Clinical Foundations of Musculoskeletal Medicine

A Manual for Medical Students

Robert J. Esther
Editor

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Preface

Musculoskeletal diseases are a significant source of morbidity. Students, however, often receive scant formal education in musculoskeletal anatomy and pathology. A foundational knowledge of the musculoskeletal system is important not only in orthopedic surgery and rheumatology, but also in a wide range of other specialties. Given the prevalence of musculoskeletal complaints, one can make a compelling case that understanding the pathology of these conditions is particularly relevant to primary care.

The University of North Carolina School of Medicine has long been a leader in musculoskeletal education. In the 1970s, Frank Wilson, MD, and H. Robert Brashear, MD, developed a comprehensive, innovative educational program that fostered the development of generations of UNC students. Although they were orthopedists, Drs. Wilson and Brashear ensured that students of all disciplines learned the basic science and principles fundamental to sound musculoskeletal care.

Over time, the school of medicine at UNC has continued to support MSK education. The contributors to this book represent a wide range of departments and divisions. This breadth of engagement speaks to the faculty's commitment to education across a range of disciplines and specialties.

My goal is for this book to serve as an introduction for students to the various principles and science underlying musculoskeletal care. I hope that the material sparks students' interests to pursue further education in this area regardless of their chosen medical specialty. I am grateful to my co-authors and to my colleagues for inspiring me to improve as a teacher and physician.

Chapel Hill, NC, USA — Robert J. Esther

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Part I

Principles of Musculoskeletal Health and Disease

1 Incidence and Prevalence of Musculoskeletal Disease

Joshua A. Shapiro

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Goals and Objectives

- *Goal*: To introduce the reader to the incidence and prevalence of musculoskeletal disease
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Epidemiology of common musculoskeletal disease
  2. Supply and demand mismatch in musculoskeletal medicine
  3. Socioeconomic burden of musculoskeletal disease
  4. The direct and indirect expenditures associated with musculoskeletal disease
  5. Development of effective musculoskeletal medicine education

1.1 Epidemiology of Musculoskeletal Conditions

Musculoskeletal disease is demonstrating a precipitous increase in diagnosis in both the United States and globally and is among the most debilitating of all nonfatal diseases [1, 2]. Contributing to this increase is an upward trend in longevity. The average life expectancy was 68.6 years globally and 79.8 years in the United States in 2015; however, this pales in comparison with recent data that suggests that the life expectancy could reach as high as 76.2 years and 93.9 years, respectively, by the year 2050 [2, 3]. Since more than half of the US population experiences a musculoskeletal

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disorder, it is no surprise that a similar upward trend in diagnosis is expected.

Due to an increase in life expectancy, the US population is collectively aging. The United States Census Bureau projects that the number of individuals older than the age of 65 years is expected to double from the current 47.8 million to nearly 100 million by the year 2060 [3], and the MacArthur Foundation Research Network projects that this number may be reached as soon as the year 2050 [4]! Despite this, the 2016 census conducted by the American Academy of Orthopaedic Surgeons estimated that there are only 29,613 practicing orthopedic surgeons in the United States, demonstrating a massive underrepresentation in surgical care of musculoskeletal disease, with an estimated shortage of 5050 orthopedic surgeons by the year 2025 [5, 6]. Arkansas, West Virginia, Nevada, Mississippi, and Texas have among the lowest surgeon density in the United States at 8 surgeons per 100,000 individuals, while Wyoming, New Hampshire, Montana, Vermont, and Alaska have among the highest surgeon density at just 13 per 100,000 individuals [5]. Additionally, the American College of Rheumatology estimated that there are 5000 practicing rheumatologists in the United States, or the equivalent of 1 rheumatologist per 50,000 adults, with an estimated shortage of 2500 rheumatologists by the year 2025 [7].

Musculoskeletal disease was diagnosed in approximately 120 million adults in 2016, equivalent to roughly 1 diagnosis for every 2 American adults over the age of 18 [1, 2]. This number is higher than the rate of circulatory disease, which includes heart disease, hyperlipidemia, and hypertension, and is twice that of respiratory conditions including chronic obstructive pulmonary disease and asthma. The rate of reporting musculoskeletal complaints is similar between genders – 47% of men will report a musculoskeletal complaint compared to 53% of women. The incidence of a new musculoskeletal diagnosis peaks in middle age, compared to the incidence of new circulatory and respiratory conditions which both peak by age 75. Akin to other medical conditions, non-Hispanic Whites and those who reside in the Midwest report the highest prevalence of musculoskeletal disease, and those with occupations in construction, office and administrative support, healthcare, and environmental services are more likely to develop musculoskeletal disease [2].

The following subsections will review the incidence of general musculoskeletal conditions. For a more complete overview of the conditions, reference the corresponding chapter.

Back and Neck Pain Back and neck pain are reported to affect nearly one in three adults in the United States annually. Over one-third of those who reported back pain reported concomitant radiating leg pain consistent with a syndrome of radiculopathy [2].

Osteoarthritis Nearly one-quarter of the US adult population suffers from degenerative arthritis of the shoulder, elbow, wrist, hand, hip, knee, ankle, foot, or spine. Not surprisingly, osteoarthritis has a higher prevalence in older individuals, afflicting nearly 50% of the population over the age of 65. Persons of non-Hispanic White ethnicity and those who reside in the Midwest report higher rates of arthritis [2].

Rheumatoid Arthritis and Other Inflammatory Conditions The prevalence of rheumatoid arthritis is approximately 0.3–1.0% worldwide [8]. Septic arthritis of native joints has an estimated annual incidence of 0.002% [9]. Gout, a crystalline arthropathy, has doubled in incidence over the past 20 years to an estimated 0.12–0.15% annually. This rise in crystalline disease has been attributed to an increasing prevalence of comorbid medical conditions including hypertension, diabetes mellitus, renal disease, hyperlipidemia, and morbid obesity [10].

Chronic Arthralgias Excluding axial skeleton pain, chronic joint pain is reported by nearly 30% of adult Americans. Chronic knee pain is the most common reported arthralgia and is seen in approximately one-quarter of middle-aged Americans. Approximately one-third of those older than 65 years of age report chronic knee pain, and each year, over 600,000 total knee replacements are performed in the United States [11].

Osteoporosis and Related Conditions Osteoporosis is defined as a T-score less than −2.5, signifying an individual whose bone density is 2.5 standard deviations below the average bone density of the entire population, and is also diagnosed in any individual who suffers a fragility fracture (e.g., distal radius, vertebral body, proximal femoral, or distal femoral fracture after a low-energy mechanism such as fall from standing height). Osteoporosis is estimated to affect more than 10 million people in the United States, and the lifetime incidence of a fragility fracture is estimated to be 40–50% in women and 13–22% in men [12, 13].

Injuries Approximately two-thirds of all injuries involve the musculoskeletal system. In 2011, 65.8 million musculoskeletal injuries from high- and low-energy trauma, workplace incidents, sports-related injuries, and military injuries were reported. This represented approximately two-thirds of the 85.1 million total reported injuries that year [14].

Fractures Fractures in adult males demonstrate a bimodal age distribution that peaks at 2.19 fractures per 100 person-years between years 12 and 19 and 2.32 fractures per 100 person-years between years 90 and 99. In contrast, there is a uniform incidence of 0.8 fractures per 100 person-years in pre-menopausal women. However, the incidence skyrockets to 4.97 fractures per 100 person-years in women aged 90–99 years [15]. Different fractures demonstrate varying distributions among age and gender, owing to changes in activity and bone quality as we age. The most common fractures in adults are of the distal radius, metacarpals, proximal femur, finger phalanges, and ankle. The least common are of the sesamoids, talus, scapula, distal femur, and midfoot [15].

Athletics According to the Centers for Disease Control and Prevention, approximately 4.3 million sports and recreation-related injuries are treated annually in the United States. It is estimated that 30 million children and 150 million adults participate in some form of athletics each year [16].

Work-Related Nearly 1 million work-related injuries and illnesses are reported by the United States Department of Labor annually. Of those, 30% are due to musculoskeletal injury [14].

Military In the military, over 600,000 annual visits occur annually for musculoskeletal injuries and injury-related conditions [14].

Neoplasms 3400 people will be diagnosed with a malignant neoplasm in the United States, or approximately nine in every one million individuals, annually. Approximately 0.1% of men and women will be diagnosed with a malignant bone neoplasm in their lifetime [17].

Pediatrics Pediatric musculoskeletal trauma was diagnosed 12.9 million times in 2012. Nearly 15% of that is a result of sports-related injury. Amazingly, fractures constitute up to one-quarter of all pediatric injuries, and 42% of boys and 27% of girls will sustain a fracture during their childhood and teenage years [18]. Musculoskeletal infection including septic arthritis and osteomyelitis is diagnosed over 100,000 times annually in children. Musculoskeletal deformity, including scoliosis, is diagnosed 1.8 million times annually, neuromuscular conditions including cerebral palsy are diagnosed over 600,000 times annually, and skeletal dysplasia is diagnosed in 2–5 per 10,000 live births annually. The incidence of pediatric rheumatologic conditions is approximately 300,000 annually. The incidence of primary pediatric musculoskeletal neoplasms is approximately 140,000 per year [12, 14, 19, 20].

The burden of musculoskeletal diagnosis is profound. With projections estimating a steady rise in the most vulnerable populations, musculoskeletal disease will continue to be a major player in domestic and global medicine for years to come.

1.2 Socioeconomic Impact of Musculoskeletal Disease

The United States spends approximately 17.8% of its gross domestic product (GDP) on healthcare each year. Amid an aging and ageless population, musculoskeletal medicine grew from a modest 3.4% share of the US GDP in the 1990s to 5.7% in 2011, representing nearly one-third of all healthcare dollars spent, and equating to an estimated $874 billion [1]. Americans will make an average of six ambulatory physician visits per person for treatment of a musculoskeletal condition annually. Over half of these individuals will average 4.5 office visits each year to a nonphysician healthcare provider, including advanced practice practitioners (nurse practitioners and physician assistants), physical and occupational therapists, and chiropractors. 12% of patients with a musculoskeletal condition require inpatient admission annually. 5.5% of patients with a musculoskeletal condition require on average 3.7 home health visits from nurses and therapists to assist in treatment and recovery. The direct healthcare expenditure for an individual diagnosed with a musculoskeletal condition is estimated to be over $8200 [14].

The treatment of musculoskeletal conditions often necessitates significant time removed from the workface or even a complete change in occupation to accommodate a new disability. Recall that those with labor-intensive occupations including those in construction, healthcare, and environmental services are more likely to develop musculoskeletal disease, and these individuals may not be physically able to perform tasks required by their occupation during treatment and recovery. In fact, musculoskeletal disorders are routinely among the top ten contributors of years lived with disability (YLD) in both men and women in the United States. Chronic low back pain is the number one cause of YLD for both genders, neck pain is in the top six for both genders, and other musculoskeletal conditions, including arthritis and trauma, are routinely found in the top ten contributors to YLD [2]. Astoundingly, the annual lost wages attributed to recovering from a musculoskeletal condition are estimated to be over $150 billion, which is nearly 1.6x the average wage lost for all other medical conditions combined. That means that in addition to direct healthcare costs, the working individual with a musculoskeletal disease may lose approximately $2500 in lost wages. When this indirect expenditure is combined with direct healthcare expenditure, the total estimated cost of musculoskeletal disease in the United States nears one trillion dollars annually [14, 21]!

1.3 Developing Quality Education in Musculoskeletal Medicine

The need for improvement in musculoskeletal education is widely known. Even though greater than half of the population will be diagnosed with a musculoskeletal condition, nearly $900 billion will be spent on treating musculoskeletal disorders, and nearly $150 billion work wages will be lost to musculoskeletal disease [14, 21], graduating medical students often feel unprepared to diagnose and treat musculoskeletal conditions. In the early 2000s, only 2% of medical school curriculum was devoted to musculoskeletal medicine, and one-third of medical students were not exposed to the diagnosis or treatment of musculoskeletal disease in medical school [22]. Astonishingly, only 10–29% of graduating medical students were able to pass an examination put forth by Freedman and Bernstein, and validated by orthopedic surgery residency program directors, of basic competencies required of all, not just orthopedic, first-year residents. Even though those who completed a musculoskeletal course scored 12–24% higher than their counterparts, the failure to graduate US medical students competent in musculoskeletal medicine was evident [23]. To validate their results, Freedman and Bernstein surveyed internal medicine residency program directors who generally agreed with the competencies expected of a graduating medical student set forth by their orthopedic surgery program director counterparts. Despite this, over three-quarters of first-year medicine and surgery residents failed to demonstrate basic competency

in musculoskeletal medicine, and the authors concluded that both quantitative and qualitative deficiencies existed in musculoskeletal education [23]. Around the same time, reports from multiple medical schools demonstrated that in the absence of a dedicated musculoskeletal course, there was a significant reduction in a student's confidence in his or her ability to perform a physical examination of the musculoskeletal system compared to his or her confidence in performing a respiratory exam [24, 25]. However, students who completed a musculoskeletal course demonstrated statistically significant increases in both their confidence and competency for evaluating musculoskeletal conditions [24, 25].

Amid the increasing socioeconomic demand posed by musculoskeletal disease, the World Health Organization, endorsed by the United Nations, declared 2000–2010 "The Bone and Joint Decade" in an effort to promote worldwide initiatives in humanitarian and educational efforts through a new level of collaboration between patient, provider, research, government, and industry [26]. In accordance with this, members of the US Bone and Joint Decade Campaign, Association of American Medical Colleges, American Academy of Orthopaedic Surgeons, American Society for Bone and Mineral Research, American College of Rheumatology, and American Academy of Physical Medicine and Rehabilitation met at the Musculoskeletal Medical Student Educators' Workshop and identified 18 educational objectives that should be met by medical students prior to graduation (Table 1.1). Chiefly among those were the abilities to perform a musculoskeletal physical exami-

Table 1.1 Objectives for undergraduate medical education in musculoskeletal medicine from the 2003 Musculoskeletal Medical Student Educators' Workshop [27]

1. Demonstrate the ability to perform an appropriate musculoskeletal history and physical examination
2. Develop an organizational framework for the diagnosis and treatment of patients presenting with low back pain
3. Discuss the impact of aging on musculoskeletal health
4. Recognize and initiate appropriate treatment for the following musculoskeletal emergencies: septic arthritis, necrotizing fasciitis, compartment syndrome, open fracture, cauda equina syndrome, and joint dislocation
5. Develop an organizational framework for the diagnosis, initial management, and definitive management of patients with fractures of the axial and appendicular skeleton
6. Develop an organizational framework for the diagnosis and treatment of patients presenting with osteoarthritis
7. Develop an organizational framework for the diagnosis and treatment of patients presenting with rheumatoid arthritis
8. Develop an organizational framework for the diagnosis and treatment of patients presenting with crystalline arthritis: gout and pseudogout (calcium pyrophosphate)
9. Develop an organizational framework for the diagnosis and treatment of patients presenting with sports injuries (both chronic overuse phenomena and acute injury)
10. Develop an organizational framework for the diagnosis and treatment of patients presenting with occupational injury (both acute and chronic overuse phenomena and injury)
11. Develop an organizational framework for the diagnosis and treatment of patients presenting with musculoskeletal infection
12. Develop an organizational framework for the diagnosis and treatment of patients presenting with musculoskeletal neoplasia (both primary and metastatic diseases)
13. Understand the relevant physiologic, pathologic, and sociologic issues involved in the treatment of patients with spinal cord injury or stroke
14. Understand the relevant physiologic, pathologic, and sociologic issues involved in the treatment of children with myopathic or neurologic conditions and in the treatment of complicating neuromuscular problems in adults with diabetes mellitus
15. Understand the relevant physiologic, pathologic, and sociologic issues involved in the treatment of children with orthopedic disorders
16. Display an understanding of the diagnosis and treatment of patients suffering from chronic pain and of the interdisciplinary approach required for the treatment of this condition
17. Understand normal and abnormal physiologic characteristics of bone and the clinical presentation and treatment of patients with bone that has altered physiologic properties
18. Demonstrate an understanding of the principles and practice of injury and disease

nation and to diagnose common musculoskeletal conditions. However, at that time, only 42% of medical schools in the United States had a required preclinical course in musculoskeletal medicine, and only 20.5% had a required musculoskeletal clinical clerkship [22].

The release of these reports instigated an institutional change in medical student education. At the end of the Bone and Joint Decade, nearly 80% of medical schools in the United States required a musculoskeletal preclinical course compared to just 42% at the beginning of the decade. Moreover, the percentage of US medical schools that required a clinical clerkship in musculoskeletal medicine increased by 4% [28]. In total, medical schools demonstrated a 34–91% increase in class time dedicated to a new musculoskeletal curriculum [29, 30].

In addition to a quantitative increase, medical schools began to implement a variety of instructional tools to improve the quality of musculoskeletal education to match the objectives developed at the 2003 Musculoskeletal Medical Student Educators' Workshop. The University of North Carolina School of Medicine developed an educational program with an emphasis on four teaching objectives: (1) normal development structure and function of the musculoskeletal system; (2) normal physiology and biochemistry of the bone, cartilage, synovium, and muscle; (3) pathologic changes produced in the bone, cartilage, synovium, and muscle by injury or disease; and (4) correlations among the pathologic, radiographic, laboratory, and clinical aspects in patients with musculoskeletal disorders. To impart this knowledge, a multidisciplinary and multifaceted approach, including additional coursework in the anatomy lab, a focus on small group sessions and case presentations, and a refined lecture series focused on competencies agreed upon by internists, rheumatologists, and orthopedists, was used. The emphasis on these objectives was validated by a substantial increase from pretest, 32.33% average, to posttest, 76.74% average, scores [31]. The University of Minnesota Medical School implemented a similar multidisciplinary preclinical course with content delivered through lecture, case presentations, and small group sessions. Their students demonstrated marked improvement in test scores and confidence levels in evaluating musculoskeletal conditions [32]. The Louisiana State University School of Medicine too developed a similar course with additional focus on anatomy laboratories. Their first-year medical students scored an average of 77.8% on the Freedman and Bernstein examination, a marked increase from the 59% average that Freedman and Bernstein found in first-year *residents* in 1998 [23, 33]. A combination of high quality of course objectives, multidisciplinary approach, and multifaceted settings allowed these schools to excel in musculoskeletal education.

As the world's population continues to age, so too will the socioeconomic impact of musculoskeletal disease. It is of utmost importance for the developing medical student to achieve competency in evaluating and diagnosing musculoskeletal disease. The objectives are clear and the education system has risen to the challenge. It is now up to the student to learn and excel.

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2 Musculoskeletal Tissues and Anatomy

Kurt O. Gilliland and Edward T. Kernick

Contents

Goals and Objectives

- *Goal*: To introduce the reader to musculoskeletal tissues and anatomy
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Skeletal system including bones and joints
  2. Cellular structure of cartilage and bone
  3. Muscular system including muscles, tendons, and ligaments
  4. Cellular structure of skeletal muscle

The skeletal system has multiple functions including protection of vital organs, contributing to posture, serving as a reservoir for calcium and phosphorus, housing cells which develop into blood cells, and serving as locations on which muscles act to produce the movements permitted by the joints. The bones that form the skeletal system are classified according to shape into short, flat, sesamoid, irregular, and long bones. These bones, approximately 206 in number in the adult, are too numerous to name and describe in a single chapter but can be discussed accord-

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ing to their general shapes. *Short bones*, which are cuboid in shape, include the eight carpal bones in each wrist and the seven tarsal bones in each foot. They are composed of spongy bone and marrow surrounded by a thin outer layer of compact bone. *Flat bones*, which consist of two layers of compact bone enclosing spongy bone and a marrow space known as diploe, include the bones in the calvaria of the skull (e.g., frontal, occipital, parietal, and the squamous portion of the temporal bone) as well as the ribs, sternum, and scapulae. They are unique in that they have articular surfaces that are covered with fibrocartilage. *Sesamoid bones*, which are shaped like sesame seeds, are located where tendons cross the ends of long bones in the limbs, as in the wrist and the knee (e.g., patella). These bones reduce friction on the tendon, thus protecting it from excessive wear. *Irregular bones*, which contain mostly spongy bone enclosed by a thick outer layer of compact bone, include various bones of the skull base (e.g., sphenoid and ethmoid bones), facial bones (e.g., maxilla), hips, and vertebrae. Finally, *long bones* are composed of a diaphysis, a shaft which has an outer region of compact bone and inner medullary cavity containing bone marrow. At each end of a long bone is an epiphysis which is composed of spongy bone surrounded by a thin layer of compact bone and which is separated from the diaphysis by the epiphyseal growth plate. The metaphysis is the part of the diaphysis adjacent to the epiphysis and serves as a region of growth during bone development (Fig. 2.1). Long bones include the clavicle (the only long bone to form intramembranously), humerus, radius, ulna, metacarpals, and phalanges in the upper limb and the femur, tibia, fibula, metatarsals, and phalanges in the lower limb. Finally, there are other specialized bones such as the small bones of the middle ear (e.g., the malleus, incus, and stapes) [1, 2].

2.1 Joints

Joints, which are locations where two or more bones are united, are classified based on structural features. *Fibrous joints* (also known as synarthroses) have no joint cavities, are joined by fibrous connective tissue, and permit little movement. Sutures are specialized fibrous joints connecting the flat bones of the skull to one another, whereas syndesmoses are the fibrous joints that are located, for example, between the tibia and fibula near the ankle joint and between the stapes and oval window in the middle ear. *Cartilaginous joints* have no joint cavity and are joined by cartilage instead of simply fibrous connective tissue. Primary cartilaginous joints (also known as synchondroses), which are joined by hyaline cartilage, allow no movement but do allow growth as long bones grow at the epiphyseal plate. The manubriosternal and spheno-occipital joints are also classified as primary cartilaginous joints. Secondary cartilaginous joints (also known as symphyses), which are joined by fibrocartilage, allow a small amount of movement. Intervertebral disks and the pubic symphysis are secondary cartilaginous joints. *Synovial joints* (sometimes known as diarthrodial joints) are composed of an articular (joint) cavity with inner surfaces lined by hyaline articular cartilage. These joints are surrounded by a two-layered capsule. The external layer is a tough, fibrous layer of dense connective tissue, whereas the internal layer, or synovial membrane, is lined by a layer of squamous to cuboidal epithelial cells on its internal surface. The epithelial layer consists of phagocytic cells and fibroblast-like cells that secrete synovial fluid which is a colorless, viscous fluid composed of proteins and hyaluronic acid. The two-layered capsule encloses the articular cavity in which the bony surfaces forming the joint are lined by hyaline articular cartilage. Synovial joints allow extensive movement and are classified according to shape and movement (Fig. 2.2) [1, 2].

There are six types of synovial joints. *Plane (gliding) joints* are locations where two flat articular surfaces come together with one bone gliding over the other. Examples include the acromioclavicular, sternoclavicular, intercarpal, carpometacarpal, and intermetacarpal joints in the upper limb and the proximal tibiofibular and intertarsal joints in the lower limb. *Condylar (ellipsoidal) joints* are composed of two convex

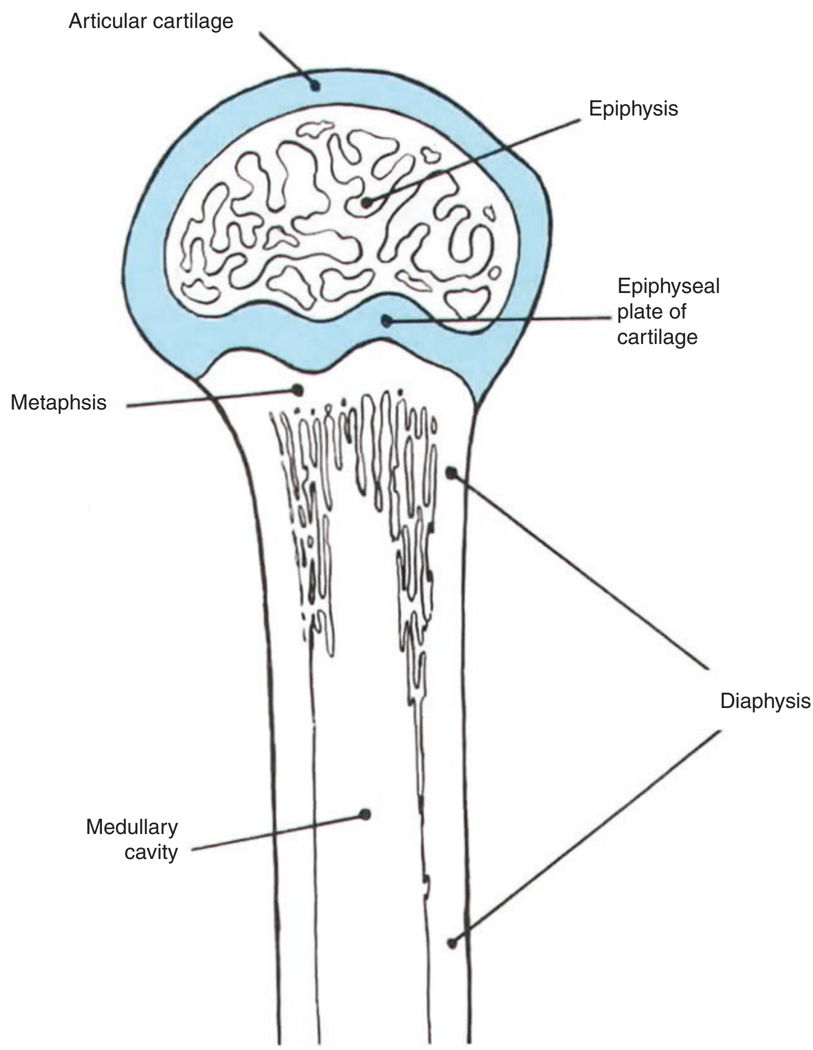

Fig. 2.1 The parts of a growing long bone. A long bone is composed of a diaphysis (shaft) which contains an inner medullary cavity of bone marrow. At the end is an epiphysis composed of spongy bone and separated from the diaphysis by the epiphyseal plate of cartilage (growth plate). The metaphysis is the part of the diaphysis adjacent to the epiphysis and serves as a region of growth during bone development. Articular cartilage, which is hyaline cartilage, is found on the surface of the end of a long bone. (From *Anatomy as a Basis for Clinical Medicine* by E.C.B. Hall-Craggs)

condyles projecting into two concave condyles, resulting in flexion and extension. These joints are found in the atlanto-occipital joints of the vertebral column; the radiocarpal and metacarpophalangeal joints of the upper limb; and the tibiofemoral joint of the lower limb. *Pivot (trochoid) joints* are unique in that part of one bone pivots within the ring of another bone, producing rotation. These joints are found in the atlantoaxial joint of the cervical vertebral column and in the superior and inferior radio-ulnar joints of the upper limb. *Hinge (ginglymus) joints*, which allow flexion and extension in a hinge-like fashion, are found in the elbow, ankle, and interphalangeal joints. *Saddle (sellar) joints* are saddle-shaped and allow not only flexion and extension but also abduction and adduction as well as circumduction. These joints occur in the carpometacarpal joint of the thumb and between the femur and patella. Finally, *ball-and-socket (spheroidal) joints* are composed of a ball (spherical head of a bone) projecting into a socket (cuplike concavity of another bone). These joints, which permit flexion, extension, abduction, adduction, medial rotation, lateral rotation, and circumduction, are located in the glenohumeral (shoulder) joint and hip joint [1, 2].

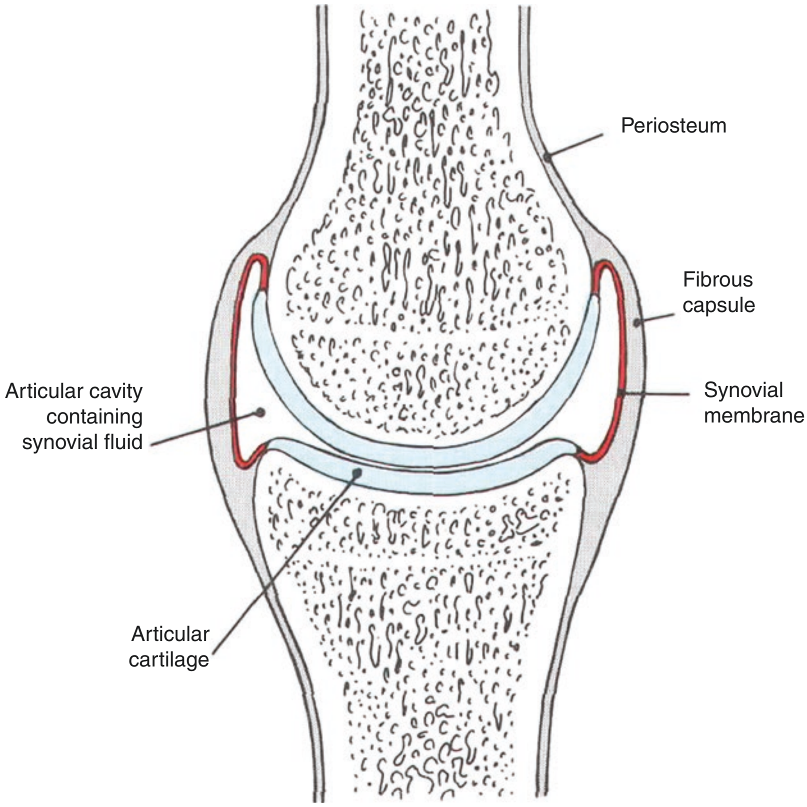

Fig. 2.2 The features of a typical synovial joint. Synovial joints are composed of an articular (joint) cavity containing synovial fluid. The inner surfaces of the cavity are lined by hyaline articular cartilage and a synovial membrane, and the joint is surrounded by a fibrous capsule. (From *Anatomy as a Basis for Clinical Medicine* by E.C.B. Hall-Craggs)

2.2 Cartilage

Cartilage is a specialized type of connective tissue that consists of chondrocytes surrounded by an extracellular matrix composed of fibers (e.g., type I or II collagen) and ground substance (e.g., chondronectin and various proteoglycans). The function of cartilage is to support surrounding soft tissues and to contribute to the development of long bones. Most but not all cartilage is surrounded by a perichondrium which contains both chondroblasts and chondrogenic cells which contribute to the development of new cartilage [2–4].

Hyaline cartilage is found in the nose, larynx, trachea, bronchi, ends of ribs, and articular surfaces of the ends of long bones; it is also involved in endochondral bone formation and the fetal skeleton. It is identified by chondrocytes arranged in isogenous groups surrounded by type II collagen (Fig. 2.3). A perichondrium, which is present for the purpose of regeneration, can be seen at the border of a cartilaginous region except on articular surfaces of bones. *Elastic cartilage* is located in the external ear, Eustachian tube, and epiglottis. It differs from hyaline cartilage in that chondrocytes are slightly

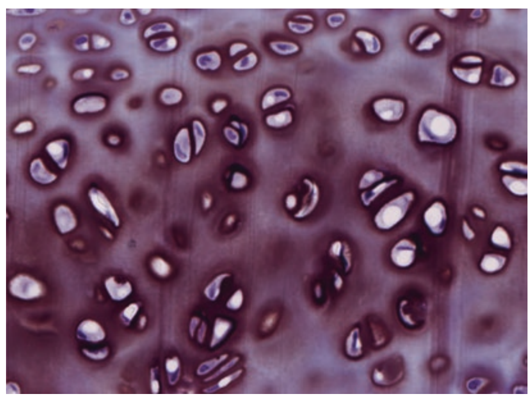

Fig. 2.3 Hyaline cartilage. This type of cartilage, which has a glassy appearance, is identified by chondrocytes arranged in isogenous groups surrounded by type II collagen

more separated from one another with surrounding extracellular matrix composed not only of type II collagen but also of elastic fibers. Regions of elastic cartilage are surrounded by a perichondrium. *Fibrocartilage* forms intervertebral disks, articular disks, tendon insertions, the pubic symphysis, sternoclavicular joints, and the meniscus of the knee. Chondrocytes are lined up in parallel rows and are surrounded by type I collagen. There is no associated perichondrium, so this cartilage does not regenerate [2–4].

While cartilage itself is avascular, the perichondrium does in fact contain blood vessels. The perichondrium consists of an outer fibrous layer and an inner cellular layer containing chondrogenic cells which in turn differentiate into chondroblasts. Chondroblasts are cells that produce the surrounding extracellular matrix and that mature into chondrocytes which are embedded in spaces within the extracellular matrix known as lacunae. Cartilage develops via two mechanisms: (1) interstitial growth (division of chondrocytes) and (2) appositional growth (differentiation of cells in the perichondrium) [2–4].

2.3 Bone

Bone is a specialized type of connective tissue that consists of osteocytes surrounded by an extracellular matrix composed of fibers (e.g., type I collagen) and ground substance (e.g., keratan sulfate and chondroitin sulfate). Unlike the cartilage matrix, bone matrix is calcified. It contains hydroxyapatite crystals composed of calcium and phosphate. In addition to these crystals, it contains magnesium, potassium, sodium, bicarbonate, citrate, and several specialized matrix proteins (e.g., sialoprotein, osteocalcin, and osteopontin) that allow bone matrix and cells to bind to one another. The function of bone is to provide a mechanism for posture, protect organs, provide a location for muscle attachment, serve as a reservoir of minerals such as calcium and phosphate, and contribute to hematopoiesis in the bone marrow [2–4].

There are four types of cells in bone. *Osteoprogenitor cells*, which are small tapered cells located in the periosteum (the outer covering of bone) and the endosteum (the lining of the marrow cavity), differentiate into osteoblasts. *Osteoblasts*, when inactive, are flattened and known as bone-lining cells. When active, however, they are larger cuboidal cells synthesizing fibers (e.g., type I collagen) and ground substance (e.g., proteoglycans and glycoproteins) of the extracellular matrix. These substances are secreted initially as an uncalcified bone matrix known as osteoid. Osteoblasts communicate with one another via cytoplasmic processes connected by gap junctions. As osteoblasts continue to secrete osteoid, which in turn is becoming calcified, they become trapped in small spaces known as lacunae and are then known as *osteocytes*, which are mature bone cells. While seemingly isolated, osteocytes receive nutrients via their surroundings and via connections with other osteocytes [2–4].

Whereas osteoprogenitor cells, osteoblasts, and osteocytes are responsible for building bone, the remaining cell type, the *osteoclast*, resorbs or breaks down bone by osteolysis. These cells, which reside in small depressions of bone known as Howship's lacunae, are large, multinucleated, and motile and are derived from the mononuclear-phagocyte system. Osteoclasts are identifiable by their acidophilic cytoplasm and ruffled border where they make contact with bone during resorption. In this region, the osteoclast decalcifies the bony surface by secreting acid followed by breaking down components of the bony matrix with enzymes such as collagenase and acid hydrolases. The remnants of these processes are absorbed by the osteoclasts and released into local blood vessels. The entire process of bone resorption is quite complex. The parathyroid gland releases parathyroid hormone (PTH), which travels through the blood to reach osteoblasts which possess PTH receptors. Osteoblasts in turn release an osteoclast-stimulating factor to promote osteoclast formation [2–5].

Bone cells and their surrounding matrix can be organized differently throughout life. Early in fetal development (and during bone repair, as well), osteocytes are surrounded by type I collagen in irregular arrangements with low calcium.

This immature bone is known as *woven bone or primary bone*, which is modified and replaced by a mature bone known as *lamellar bone or secondary bone*. The conversion of primary bone to secondary bone occurs throughout the body except in a few locations such as sutures connecting bones of the skull and locations where tendons connect to bones. Secondary bone is found in two forms, spongy and compact. *Spongy, or cancellous, bone* is found surrounding bone marrow cavities and is formed by small partitions of bone known as trabeculae which are lined by osteoblasts. Spongy bone is surrounded by compact bone which is solid with no intervening spaces containing bone marrow. *Compact bone* is composed of numerous osteons (Haversian systems) which are long parallel columns made of lamellae, which in turn are concentric rings of bone surrounding a Haversian canal (a central region for blood vessels). Volkmann canals are small channels that convey blood vessels between Haversian canals and from the periosteum to the endosteum (Fig. 2.4) [2–5].

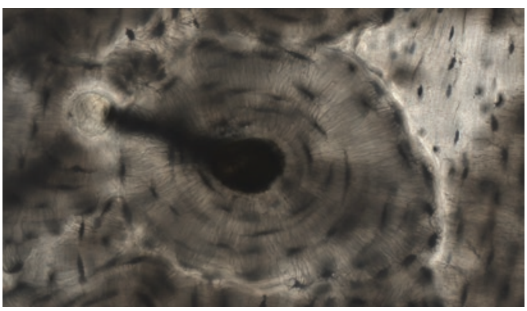

Fig. 2.4 Compact bone. Compact bone is composed of numerous osteons (Haversian systems) which are long parallel columns. One osteon is seen here cut in a cross section. It is formed by lamellae, which are concentric rings of bone surrounding a Haversian canal (a central region of the osteon for blood vessels, represented here as a black circle). Radiating out at the 10:00 position of the osteon is a Volkmann canal, which is a small channel that conveys blood vessels between Haversian canals and from the periosteum to the endosteum. The small black specks are lacunae in which osteocytes are situated. With care, one can see the canaliculi connecting these osteocytes to one another

2.4 Bone Formation

Bone formation occurs in two different ways: intramembranous formation and endochondral formation. *Intramembranous formation*, which is much simpler, occurs in the flat bones of the skull. Mesenchymal stem cells, or multipotent stromal cells, gather together, differentiate into osteoblasts, secrete osteoid which becomes calcified, and become known as osteocytes once they are surrounded by bone matrix. The result of this process creates interconnected ridges known as trabeculae which are surrounded by blood vessels and bone marrow (Fig. 2.5) [2–4].

Endochondral formation, which is much more complex, occurs in long bones and is based on a cartilage model as a starting point (1). The process begins at a primary center of ossification located at the midpoint of the diaphysis (shaft) of a developing long bone's initial cartilage model. Blood flow to the perichondrium (outer region) causes chondrogenic cells to convert to osteoprogenitor cells which in turn differentiate into osteoblasts, thus creating a periosteum. Through intramembranous formation (the simpler form of bone formation), osteoblasts secrete components of bone matrix into their surroundings to create a

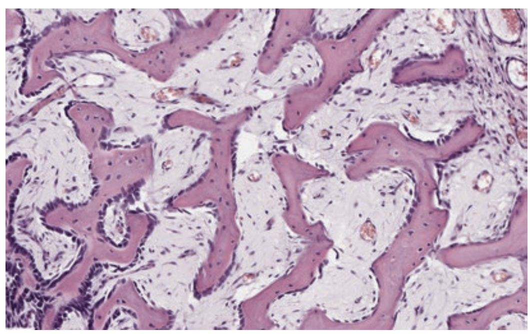

Fig. 2.5 Intramembranous bone formation. The process of intramembranous ossification is distinct from endochondral ossification. With no pre-existing hyaline cartilage, mesenchymal cells differentiate into osteoblasts (the small dark rectangular cells lining the darker interconnected regions). As the bone matrix increases and surrounds some of these osteoblasts, they become osteocytes, which can be seen within these darker regions

subperiosteal bone collar. Deeper within the cartilage model, chondrocytes undergo a process of degeneration, leaving large spaces that will later be filled with bone marrow. Osteoclasts then pierce the bone collar created earlier and create channels through which blood vessels, mesenchymal cells, and osteoprogenitor cells can enter these spaces within the cartilage model with calcification of both cartilage and newly formed bone beginning to occur, resulting in a temporary complex that is eventually resorbed by osteoclasts. The resulting space will eventually become the marrow cavity of a long bone. This process is repeated toward each epiphysis (the end of a long bone) (2). The process continues at secondary centers of ossification at the epiphysis. In a similar fashion, osteoprogenitor cells differentiate into osteoblasts which secrete bone matrix components into their surroundings and replace the cartilage of the cartilage model. This process occurs in a very organized fashion. At the epiphysis, inactive chondrocytes are found at the zone of reserve. Mitosis results in many more chondrocytes at the zone of proliferation, followed by enlargement of the chondrocytes at the zone of cell hypertrophy and maturation. These chondrocytes then degenerate and the region becomes calcified in the zone of calcification. Finally, in the zone of ossification, osteoblasts secrete a bone matrix onto the calcified cartilage resulting in a temporary complex that is eventually reabsorbed by osteoclasts and replaced by bone (Fig. 2.6) [2–4].

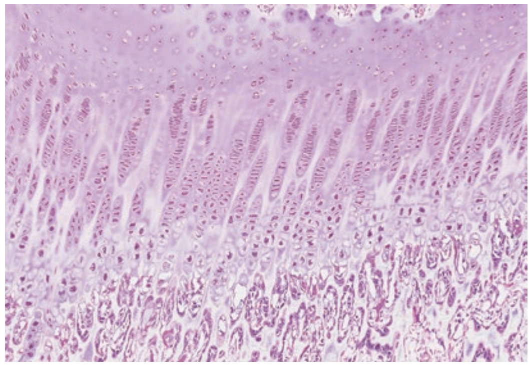

Fig. 2.6 Endochondral bone formation. At the epiphysis, inactive chondrocytes are found at the zone of reserve; note the glassy appearance of hyaline cartilage at the top of the image. Mitosis results in many more chondrocytes at the zone of proliferation; observe the increase in cell number in the upper third of the image. This process is followed by enlargement of the chondrocytes at the zone of cell hypertrophy and maturation; note the larger cells in the middle of the image. These chondrocytes then degenerate and the region becomes calcified in the zone of calcification, seen in the bottom third of the image. Finally, in the zone of ossification at the bottom of the image, osteoblasts (the small rectangular cells) secrete a bone matrix onto the calcified cartilage resulting in a temporary complex that is eventually resorbed by osteoclasts and replaced by bone

Bone, which is dynamic, is constantly being remodeled as growth occurs and as it adapts to environmental stress. Growth occurs when bone formation exceeds bone resorption. When a fracture damages the matrix, bone cells, and blood vessels, hemorrhaging and blood clot formation occur. Proliferation of osteoprogenitor cells then occurs in both the periosteum and endosteum with cellular tissue surrounding the fracture and penetrating the damaged bone. Formation of a bony callus occurs both internally and externally; fibrous connective tissue and hyaline cartilage are formed. Intramembranous bone formation also produces primary bone, and endochondral bone formation replaces cartilage with primary bone, as well. The irregularly arranged trabeculae of primary bone join the ends of the fractured bone, producing a bony callus. The primary bone is resorbed and replaced with secondary bone as healing occurs [2–4].

2.5 Muscular System

The muscular system produces movement, contributes to heat generation, and assists with posture. There are three types of muscle, smooth muscle, cardiac muscle, and skeletal muscle, the latter of which is most relevant to orthopedics. *Skeletal muscle*, which contributes to nearly half of the total body mass, is striated in cell struc-

ture and voluntary in function. A skeletal muscle typically attaches to two different bones – proximally at an origin and distally at an insertion, where the action, or movement, typically occurs. There are numerous shapes of skeletal muscle. *Quadrangular* (strap or parallel) muscles are found in the neck (e.g., infrahyoid strap muscles and sternocleidomastoid), the abdomen (e.g., rectus abdominis), hip (e.g., quadratus femoris), and thigh (e.g., sartorius). *Fusiform* muscles are spindle shaped with wide muscle bellies and include the psoas major and other muscles. *Bicipital* muscles have two heads (two origins) and include the biceps brachii and biceps femoris. *Triangular* (convergent) muscles have wide origins and narrow insertions and include the pectoralis major. *Unipennate* muscles (*uni*, one; *pennate*, feather) possess fibers only on one side of a tendon; examples include lumbrical muscles in the hand and foot, the extensor digitorum longus (the long wrist and finger extensor), and the flexor pollicis longus (the long thumb flexor). *Bipennate* muscles (*bi*, two; *pennate*, feather) possess fibers on both sides of a tendon; an example is the rectus femoris. *Multipennate* muscles (*multi*, many; *pennate*, feather) possess many fiber rows emanating from a central tendon; an example is the deltoid with its anterior, middle, and posterior fibers. *Circular* muscles are sphincter-like muscles such as the orbicularis oculi and orbicularis oris (Fig. 2.7) [1].

There are various forms of connective tissue which serve the purpose of connection and support in the musculoskeletal system. An entire muscle is enclosed by the *epimysium*, a thin layer of connective tissue. Muscles are connected to bones and cartilage by *tendons* which are fibrous bands of dense regular connective tissue (Fig. 2.8). Tendons that are expanded, broad, and sheet-like are known as *aponeuroses* and are often associated with flat muscles. Near joints, numerous tendons found in parallel are often held in place by a fibrous band called a *retinaculum*; for example, flexor and extensor retinacula are located at both the wrist and ankle joints to hold tendons in place. *Synovial tendon sheaths* are tube-shaped sacs enclosing tendons and filled with synovial fluid for the purpose of reducing friction. They are found where tendons pass under ligaments or retinacula and through osseofibrous tunnels. Bones, in turn, are connected to one another or to cartilage by *ligaments* which are fibrous bands of connective tissue, as well. *Bursae* are flattened sacs of synovial membrane that contain a viscous fluid for moistening and reducing friction in an area where a tendon rubs against a bone, ligament, or another tendon. *Fascia* is a fibrous connective tissue that also serves to connect and support. Superficial fascia, also known as the tela subcutanea or hypodermis, is a loose connective tissue beneath the dermis composed of a fatty superficial layer and a membranous deep layer. This region is rich in neurovasculature and glands. Deep (investing) fascia is a sheet of fibrous connective tissue that covers and supports the muscles. It contributes to origins, insertions, retinacula, and tendon sheaths [1, 2].

2.6 Skeletal Muscle

Skeletal muscle is composed of long, thin cells known as fibers. Each cell contains numerous nuclei with peripheral locations and is composed of organized units of myofibrils, each of which is composed of end-to-end functional units known as sarcomeres. A sarcomere in turn is composed of contractile filaments whose major components are actin and myosin. A single muscle cell is surrounded by reticular fibers known as the *endomysium*. A bundle or fascicle of muscle cells is bound by a connective tissue covering termed the *perimysium*, and an entire muscle itself is covered by the *epimysium* [2–4].

There are three types of skeletal muscle cells or fibers. *Red fibers* (slow; type I; "red twitch") contract slowly and repetitively without fatiguing easily. They possess high myoglobin content, many mitochondria, and high levels of oxidative enzymes (but low levels of ATPase) and generate ATP primarily through oxidative phosphorylation. *White fibers* (fast; type 2B; "white twitch"), on the other hand, contract quickly, fatiguing easily. They possess low myoglobin content, few mitochondria, and low levels of oxidative enzymes

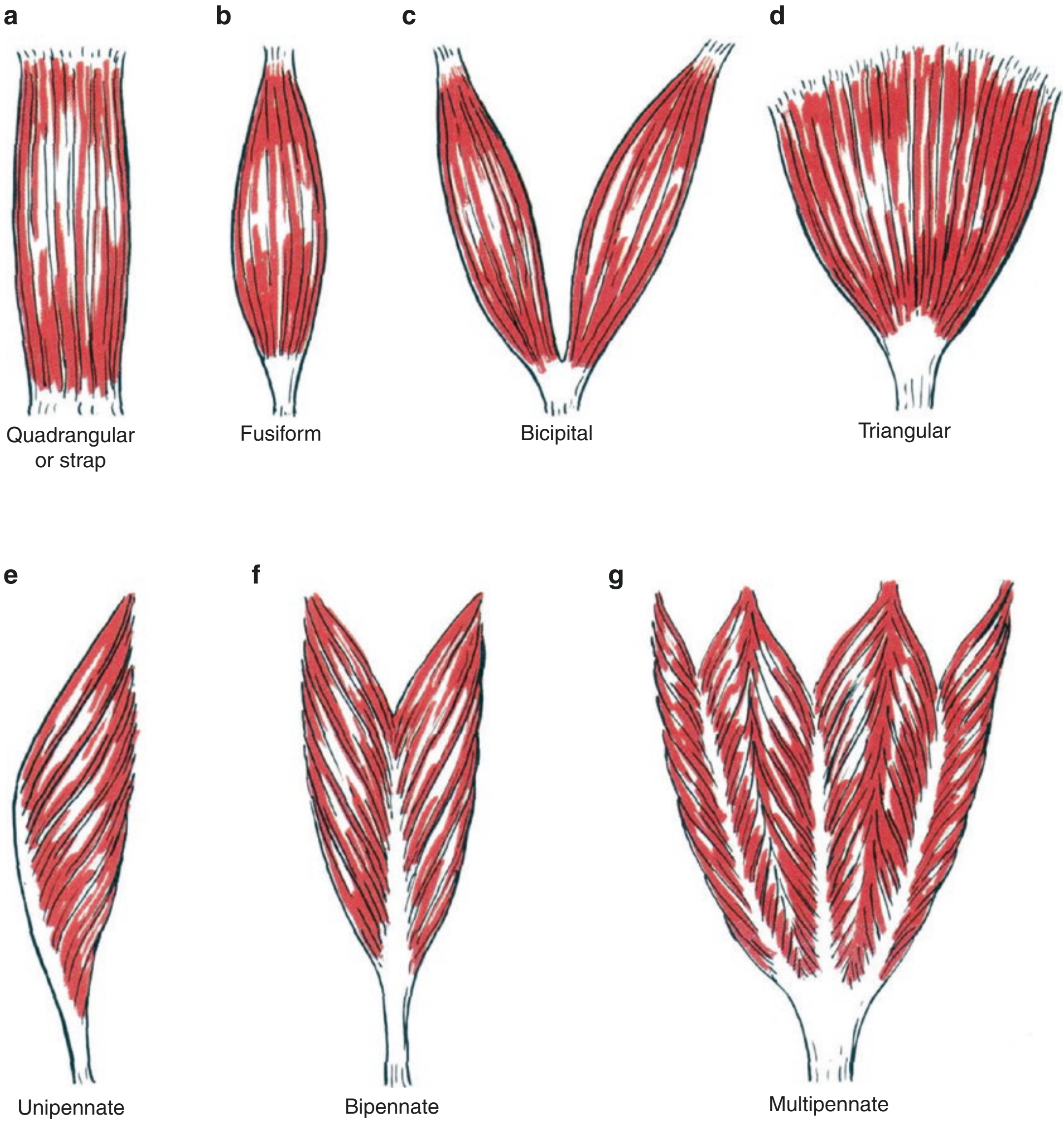

Fig. 2.7 Skeletal muscle shapes. There are numerous shapes of skeletal muscle. A. Quadrangular (parallel) muscles include infrahyoid strap muscles, sternocleidomastoid, rectus abdominis, quadratus femoris, and sartorius. B. Fusiform muscles include the psoas major. C. Bicipital muscles include the biceps brachii and biceps femoris. D. Triangular (convergent) muscles include the pectoralis major. E. Unipennate muscles include lumbrical muscles in the hand and foot, the extensor digitorum longus, and the flexor pollicis longus. F. Bipennate muscles include the rectus femoris. G. Multipennate muscles include the deltoid. (From *Anatomy as a Basis for Clinical Medicine* by E.C.B. Hall-Craggs)

(but high levels of ATPase) and generate ATP primarily through anaerobic glycolysis. *Intermediate fibers* (type 2A; "intermediate twitch"), as the name suggests, have qualities of both red and white fibers, contracting fast without fatiguing easily. They possess intermediate levels of myoglobin, some mitochondria, and intermediate levels of oxidative enzymes and ATPase and generate ATP via both oxidative phosphorylation and anaerobic glycolysis. Innervation change to a muscle fiber can result in the change of that fiber's contraction and fatigue qualities [2–4].

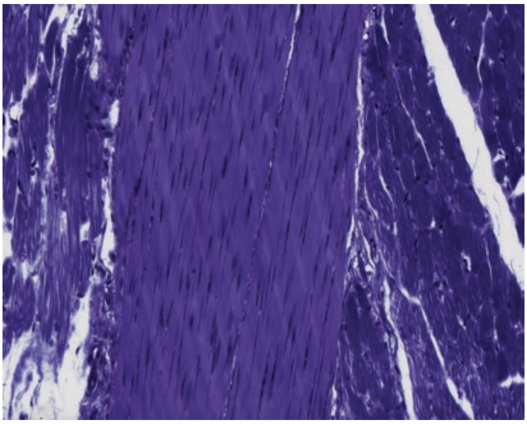

Fig. 2.8 Tendon. A tendon can be seen running vertically through the center of the image. It is composed of dense regular connective tissue. Fibroblasts (dark vertical slits) are relatively close to one another and are parallel to one another in a regular pattern, separated by an extracellular matrix. Flanking the tendon on both sides are regions of skeletal muscle

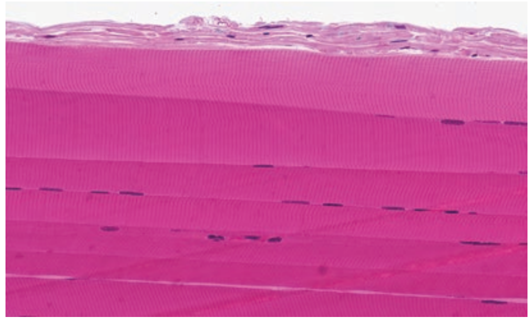

Fig. 2.9 Skeletal muscle. Approximately seven skeletal muscle cells, or fibers, can be visualized running left to right. The cells display the characteristic banding pattern. Certain regions have distinctive A bands (dark regions), I bands (light regions), and Z lines (fainter lines within the I bands). Each cell is surrounded by endomysium, but this is difficult to see. The connective tissue layer at the top of the image is epimysium. Muscle cell nuclei are located at the periphery of the cells

Skeletal muscle cells, which are surrounded by an external lamina and reticular fibers, are long and tapering cells formed by a sarcolemma (a specialized plasma membrane with tubular invaginations known as *T (transverse) tubules*) and filled with sarcoplasm (cytoplasm). They contain multiple nuclei, each of which has a peripheral location near the sarcolemma as well as numerous *myofibrils*, which are long, parallel, organized collections of contractile myofilaments (thin actin filaments and thick myosin filaments). Myofibrils are aligned such that there is a visible alternating banding pattern of A bands (dark *a*nisotropic bands) and I bands (light *i*sotropic bands). A bands contain both thick and thin filaments which overlap and interdigitate, and I bands contain only thin filaments. Six thin filaments surround each thick filament. By electron microscopy, it becomes apparent that A bands are transected by H bands (*helle* = bright) which are lighter regions where A bands consist only of thick filaments; at the center of H bands are darker regions known as M lines (*mittelscheibe* = middle of disk). The I bands are bisected by Z disks (*zwischenscheibe* = between disks). The *sarcomere* is the regular repeating region between successive Z disks and is the functional unit of contraction in skeletal muscle. During contraction, thick and thin filaments increase their overlap. Thin filaments slide past thick filaments and penetrate more deeply into the A band, which remains at constant length. I bands and H bands shorten as Z disks are drawn closer together (Fig. 2.9) [2–4].

In skeletal muscles, the smooth endoplasmic reticulum (sER) is modified such that it forms a network around each myofibril; it is known as the *sarcoplasmic reticulum* (SR). The SR, which forms a pair of expanded terminal cisternae at the junction of the A band and I band, regulates muscle contraction by releasing calcium ions for contraction and sequestering calcium ions for relaxation. The pair of SR cisternae form a complex with a centrally located T tubule; this complex is known as a triad, is located at the A-I junction, and helps provide uniform contraction throughout the cell [2–4].

The first step in muscle contraction is depolarization. The sarcolemma is depolarized at the neuromuscular junction, resulting in T tubules carrying the wave of depolarization to the myofibrils. Next, calcium is released into the sarcoplasm at the A-I junction via calcium-release channels of the SR terminal cisternae. As long as calcium levels are sufficiently high, the contraction cycle will continue. Calcium binding by troponin C results in a conformational change that

breaks the troponin I bond with actin. Tropomyosin then shifts its position slightly and uncovers the myosin-binding sites on actin filaments. This process allows myosin and actin to interact for the purpose of sliding against one another, resulting in muscle contraction. Relaxation occurs when calcium concentration in the sarcoplasm becomes low enough that troponin C loses its bound calcium. Then tropomyosin returns to its resting position, covering actin binding sites and returning the muscle to the resting state [2–4].

All of the sarcomeres of an individual muscle cell either contract in unison or do not contract at all (the "all-or-none law"). Likewise, a motor unit, which is a collection of muscle cells all innervated by the same neuron, contracts all together. Depending on how many motor units contract, an entire muscle may contract with differing degrees of strength [2–4].

Innervation of skeletal muscle occurs at the neuromuscular junction where a motor nerve axon communicates across a synapse with the skeletal muscle cell. The presynaptic membrane is depolarized resulting in the opening of voltage-gated Ca^{2+} channels. As Ca^{2+} enters the axon terminal, synaptic vesicles respond by releasing acetylcholine which binds to receptors of the postsynaptic membrane. This process results in depolarization of the sarcolemma and generation of an action potential. Acetylcholinesterase, an enzyme located in the cell membrane of the muscle cell, breaks down acetylcholine. This ends the depolarization of the muscle cell. Choline is then returned to the axon terminal to be recombined with acetyl coenzyme A (acetyl-CoA) to form acetylcholine. This process is catalyzed by choline acetyltransferase [2–4].

There are also proprioceptive receptors in skeletal muscle. The *muscle spindle* is a specialized stretch receptor for proprioception. It consists of eight to ten modified skeletal muscle cells ("intrafusal fibers," also known as flower-spray endings or annulospiral endings) surrounded by a connective tissue capsule enclosing a fluid-filled space. The surrounding normal skeletal muscle cells are "extrafusal fibers." When a muscle is stretched, the muscle spindle is stretched, activating sensory neurons which relay information about the rate and duration of the stretch. The central nervous system responds by initiating contraction to counteract the stretching. The *Golgi tendon organ*, which is located in tendons, also serves as a proprioceptive receptor. This structure consists of encapsulated collagen fibers surrounded by sensory nerves, and if stimulated the tendon is stretched due to extensive muscle contraction [2–4].

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3 Introduction to Musculoskeletal Imaging

Jordan B. Renner

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the imaging of musculoskeletal disease
- *Objectives*: On completion of this unit, the learner should be able to describe and define the:
  1. Basic technical characteristics of the different imaging modalities
  2. Applicability of different imaging modalities for the evaluation of musculoskeletal pathologies described and depicted in this unit
  3. Need for thoughtful selection of an imaging procedure of intervention in order to optimize maximize imaging efficiency

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The assessment and management of a patient with a musculoskeletal condition begin with a thorough history and physical examination. In some cases, clinical laboratory information may be helpful, and in others, neurophysiologic studies may be of value. In many cases, however, the information gained from diagnostic imaging studies is indispensable and may be central to defining the condition.

Modern diagnostic imaging includes many modalities, each with its own attributes and sensi-

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tivity and specificity. Conventional radiography, computed tomography, ultrasound, magnetic resonance imaging, nuclear medicine, and, on occasion, vascular imaging and interventional radiology may all have a place in musculoskeletal imaging. The selection of an imaging modality depends fundamentally on the clinical question to be answered. Imaging can be expensive and, for some modalities, is not without risk, so the selection of a modality that is safe and most likely to address the clinical concern will result in a cost-effective imaging evaluation. In most cases imaging begins with conventional radiography, and, in many cases, radiography may satisfy the imaging need. In other cases, further imaging is needed for complete characterization of the process at hand.

3.1 Conventional Radiography

Wilhelm Röntgen discovered the x-ray in 1895, and the first medical radiograph was of his wife's hand. Clinical imaging of fractures and localization of foreign bodies after penetrating trauma followed soon after that. The detailed evaluation of many fractures, articular diseases, and bone tumors came later.

Early conventional radiography relied on the use of light-sensitive, silver halide-containing emulsions spread on glass plates. Over time, technological improvements provided emulsions that were more sensitive than the initial compounds and allowed shorter exposure times, an important factor in minimizing radiation dose to the patient. Glass plates, obviously fragile and difficult to store, were later replaced by cellulose nitrate films. Cellulose nitrate films were flexible, lightweight, and transparent but tended to curl and buckle and were very flammable. The introduction of a plastic-based film substrate, polyethylene terephthalate, in the 1960s provided a safe, easily stored, and durable film base.

At the same time, emulsions to coat the film substrate were also improved, resulting in emulsions that provided higher-resolution imaging and were more stable and sensitive to radiation; more sensitive emulsions allowed radiation doses to be decreased. Radiation dose to the patient was reduced further through the use of intensifying screens, plastic sheets that were coated with a radiation-sensitive layer containing one of a variety of salts that fluoresced after exposure to x-rays and emitted light of a particular spectrum. Matching the spectral emission of the screen coating with the spectral sensitivity of the film emulsion was much more efficient than relying only on x-ray photons for image production and allowed much lower patient doses. An x-ray cassette contained a sheet of x-ray film, the ultimate image receptor, layered on one or both sides by an intensifying screen. At the time of the exposure, the x-ray beam leaving the body part to be imaged passed through the wall of the cassette and interacted with the intensifying screen coating. The salts in the coating absorbed a certain amount of the radiation beam and fluoresced. The resulting fluorescence was absorbed by the film emulsion. After development, the x-ray image was revealed on film.

In the past couple of decades, conventional radiography has moved beyond the film-screen radiography and has been replaced by computed radiography (CR) and digital radiography (DR). In CR, the x-ray beam leaving the patient is captured by a photostimulable phosphor plate, and a certain proportion of the x-ray photons is absorbed. The photostimulable phosphor plate is then read in a plate reader in which the plate is exposed to a laser. This process releases the absorbed energy in the photostimulable plate, and the released energy is captured generating the radiographic image. In DR, the x-ray beam leaving the patient is received by an imaging plate covered by a thin matrix of photodiodes and other electronics that captures the beam and converts it directly to a radiographic image: no film developer or CR plate reader is needed. Both CR and DR result in digital images that can be viewed, manipulated, and stored electronically. Physical sheets of film are rarely needed except in situations in which an actual-size image of the body part is needed for operative planning or templating. The term *plain film* to describe the image product of either CR or DR imaging, like the use of film-screen radiog-

raphy itself, is clearly outmoded and should be replaced by the term *conventional radiography*.

Both CR and DR provide substantial improvements in image production efficiency and storage compared to film-screen radiography. Optimal conventional radiography with CR or DR, however, still requires the proper positioning of the body part to be imaged. It is equally important that the incident x-ray beam, the beam emitted by the x-ray tube at the time of exposure, be adequately restricted or *collimated*, both to maximize image quality and to minimize patient radiation dose. The employment of a properly educated and certified radiologic technologist will help ensure that the radiography is performed as well as possible.

The sensitivity and specificity of conventional radiography vary by the disease or disorder being imaged. Fractures and dislocations in the peripheral skeleton, for example, may be adequately characterized by the radiographic findings (Fig. 3.1). Conventional radiographs are often sufficient to define the nature of the articular disease in a patient presenting with signs and symptoms of joint disease (Fig. 3.2). A patient presenting with a suspected musculoskeletal neoplasm must undergo radiography prior to other imaging. In skeletal neoplasms, in particular, conventional radiographs may be both sensitive and specific and can often predict the tumor histology quite accurately (Fig. 3.3).

In other situations, however, conventional radiographs may be of limited utility. It is well-established that the evaluation of the spine in the acutely injured patient is better done with computed tomography since conventional radiographs may fail to demonstrate clinically significant osseous injuries. In patients with low back pain, conventional radiographs may reveal abnormalities that may be associated with pain such as facet joint osteoarthritis and degenerative disc disease, but the evaluation of impingement of neural structures and other soft tissue conditions relies on the use of other modalities, often magnetic resonance imaging, discussed below.

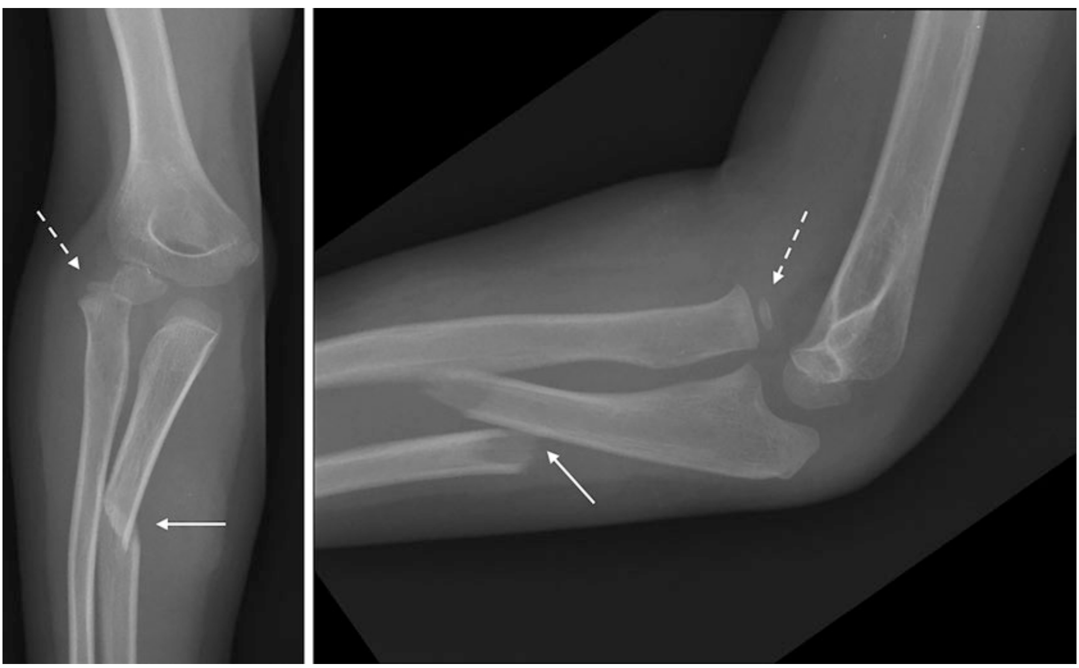

Fig. 3.1 Anteroposterior (left) and lateral (right) views of the elbow show an oblique proximal ulna fracture with posterior displacement and angulation (solid arrows) and associated anterolateral displacement of the radial head from the capitellum (dashed arrows), a Monteggia fracture-dislocation

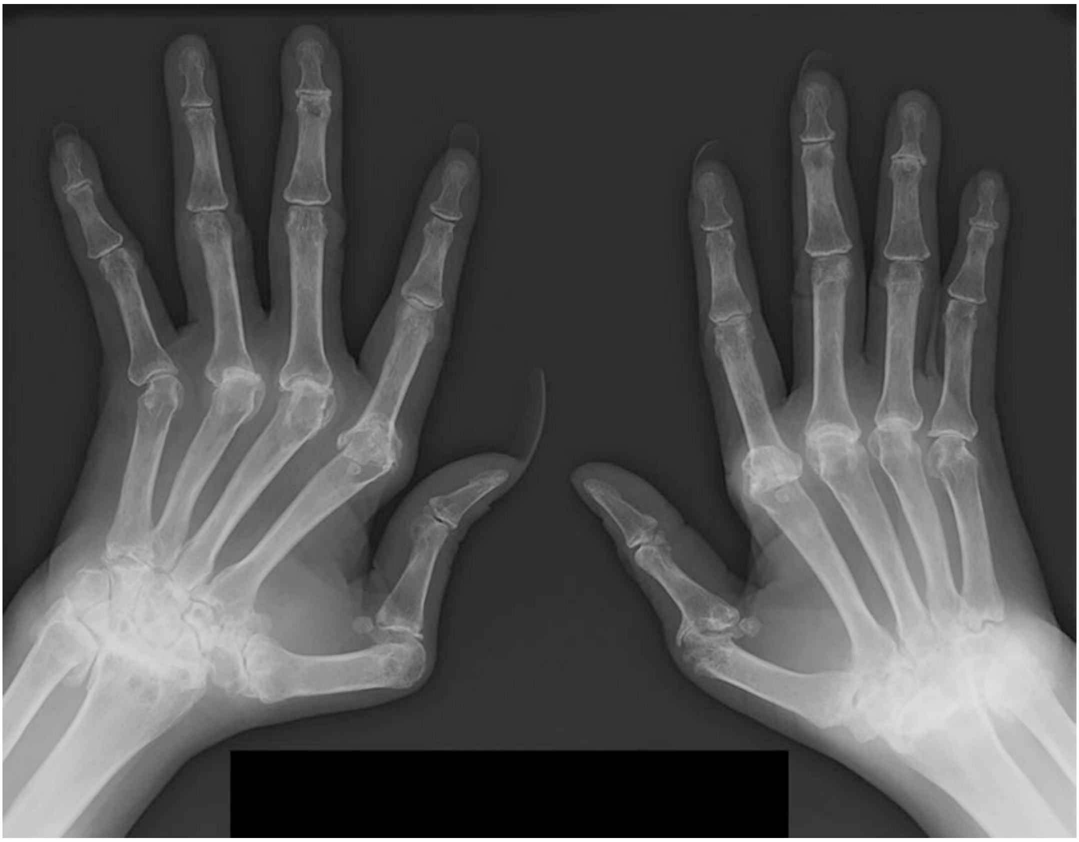

Fig. 3.2 A posteroanterior radiograph of the hands shows a symmetric arthropathy with marked narrowing of the radiocarpal, intercarpal, and metacarpophalangeal joints bilaterally. There is marked narrowing of the second through fourth metacarpophalangeal joints with ulnar deviation bilaterally. These features are typical of severe rheumatoid arthritis

3.2 Computed Tomography (CT)

Computed tomography (CT) was developed in the early 1970s: the first medical CT image was of the brain in 1971. Since that time CT has been applied to imaging all parts of the body, including the musculoskeletal system. Steady technological improvements in CT since the 1970s have resulted in current generation scanners that can produce images in less than a second, compared to hours for the early scanners. Modern CT scanners can produce images with very high spatial resolution in any anatomic plane. Dual-energy CT units can now provide enhanced imaging in patients with metallic implants such as arthroplasties by reducing metal imaging artifacts substantially.

Like conventional radiography, CT relies on x-rays for image production. In the case of CT, however, the x-ray tube generating the x-rays and the detectors that collect the x-rays that pass through the patient and that will be mathematically converted into the CT image are contained in a ring apparatus contained in the CT gantry surrounding the patient. During image acquisition, the ring rotates within the gantry around the patient, and the patient moves on a table through the gantry. The collected x-ray data are then reconstructed into whatever imaging plane is needed, and the images can be processed to emphasize soft tissue structures or bone. Radiation exposures to the patient are considerably higher with CT than with conventional radiography; unnecessary radiation exposure to the patient through

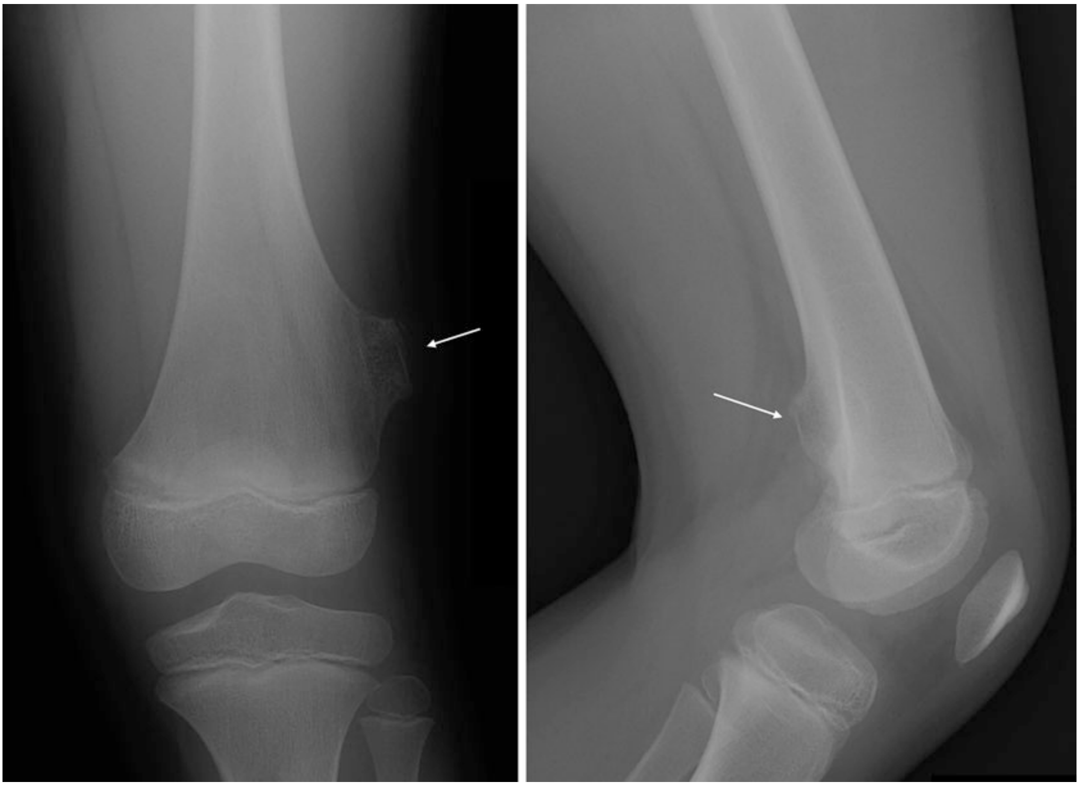

Fig. 3.3 Anteroposterior and lateral radiographs of the knee demonstrate an excrescence arising from the lateral aspect of the distal femoral metaphysis (arrows). The cortex of the underlying femur flows smoothly onto the surface of the lesion, and the trabeculae in the femur pass into the lesion, typical of an osteochondroma

the indiscriminate use of CT should be avoided, particularly in pediatric patients. In such cases, information that could be gained through the use of CT can often be obtained with either ultrasound or magnetic resonance imaging, neither of which exposes the patient to ionizing radiation.

Like conventional radiography, CT scanning results in images with excellent spatial resolution, the ability to depict tiny structures. Unlike conventional radiography, however, CT has the ability to display sectional anatomy in planes not depicted by radiography. These attributes make CT an excellent modality for the evaluation of spine trauma in which clinically significant fractures may not be depicted on conventional radiographs (Fig. 3.4). CT is also excellent for the evaluation of complex articular trauma (Fig. 3.5). In such cases CT may display the extent of bone fragmentation and articular malalignment better than radiography, and CT is better than conventional radiography at depicting intra-articular bone fragments (Fig. 3.6).

In the assessment of musculoskeletal neoplasms, CT can be helpful in displaying the extent of bone destruction. CT is also good for demonstrating the degree of calcification within the lesion (Fig. 3.7). The extent of tumor invasion of bone marrow cavities and of extraosseous tumor involvement of soft tissues and neurovascular structures is, however, better assessed with magnetic resonance imaging.

3.3 Nuclear Medicine

In musculoskeletal imaging nuclear medicine usually relies on the use of intravenously administered radiopharmaceuticals. Traditional bone scanning uses technetium-99m (^{99m}Tc) compounded with a bone-avid agent such as a phos-

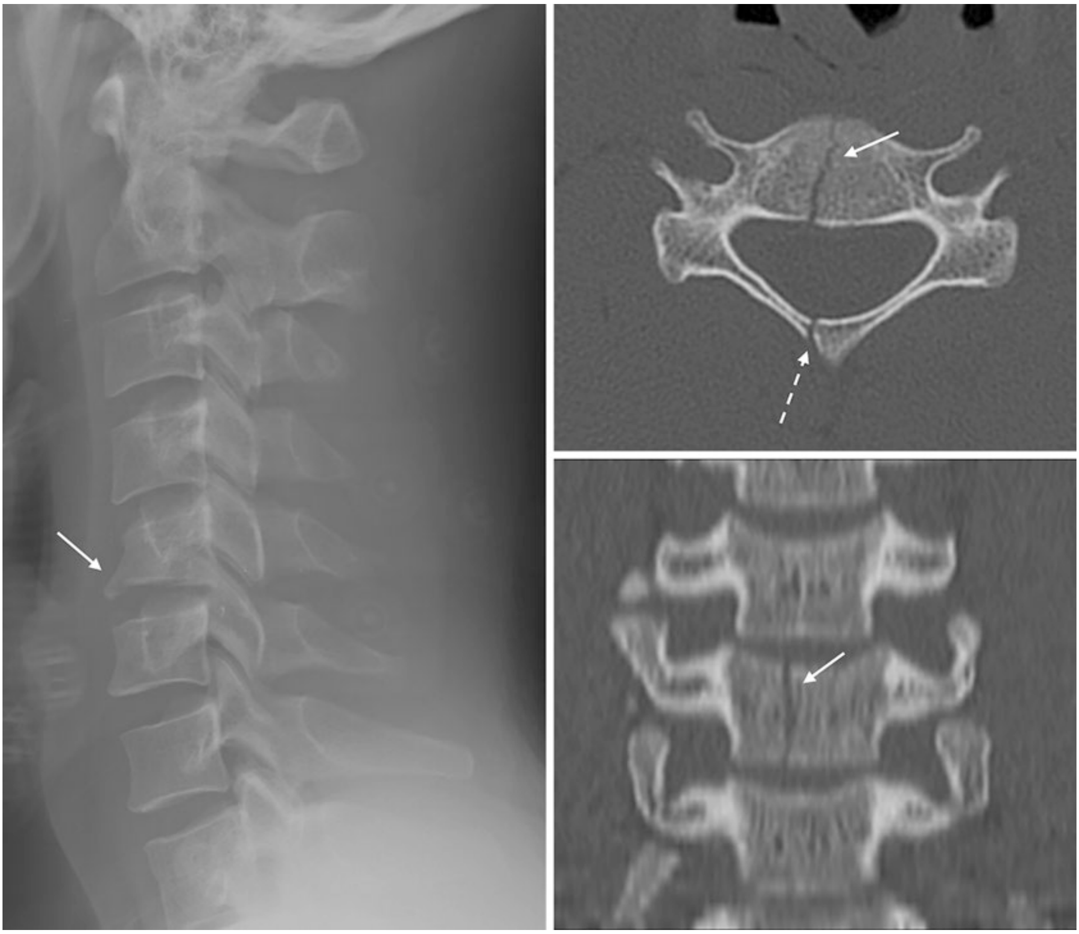

Fig. 3.4 A lateral radiograph of the cervical spine (left) shows a questionable fracture at the anteroinferior corner of the C5 vertebral (arrow). Transverse (top right) and sagittal (bottom right) CT images demonstrate a fracture extending through the C5 vertebral body centrum (solid arrows) and an associated fracture through the right C5 lamina (dashed arrow)

phonate. After injection the radiopharmaceutical is adsorbed to areas of active bone turnover. ^{99m}Tc bone scanning is very sensitive and is usually employed in the detection of metastatic disease to bone; it can readily detect metastatic deposits in bone before they are demonstrated on radiographs (Fig. 3.8). Metastatic carcinomatous or sarcomatous deposits in bone are almost always detectable by bone scanning, although the same is not true of multiple myeloma.

Stress fractures, both fatigue fractures and insufficiency fractures, are commonly encountered in clinical practice. While such injuries are usually seen in different patient populations with different histories of inciting physical activity, they are often not seen on initial radiographs at the time of presentation. Bone scanning with a ^{99m}Tc bone-seeking agent, however, can demonstrate prominent foci of abnormal accumulation, even at the time of initial presentation (Fig. 3.9), and the healing fracture can be confirmed on subsequent radiographs (Fig. 3.10).

Bone scanning, while very sensitive, may be nonspecific; any focus of active bone turn-

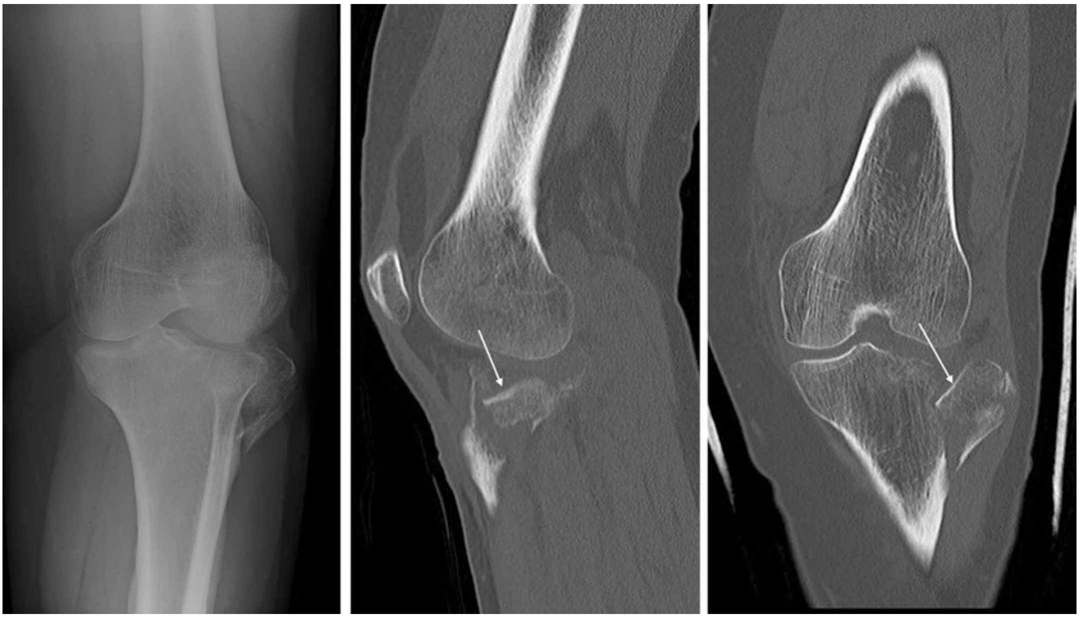

Fig. 3.5 A lateral radiograph of the knee demonstrates a comminuted lateral tibial plateau fracture. Sagittal (center) and coronal (right) CT images show the extent of impaction and inferior rotation of the articular surface fragment (arrows)

Fig. 3.6 Transverse (left) and sagittal (right) CT images reveal a posterior acetabular fracture with lateral displacement of a fracture fragment (dashed arrow). An intra-articular bone fragment is also demonstrated (arrows)

Fig. 3.7 Transverse (left) and coronal (right) CT images of the left femur. An intramedullary lesion includes multiple punctate and circular calcifications (arrows) typical of chondroid matrix calcifications in an enchondroma

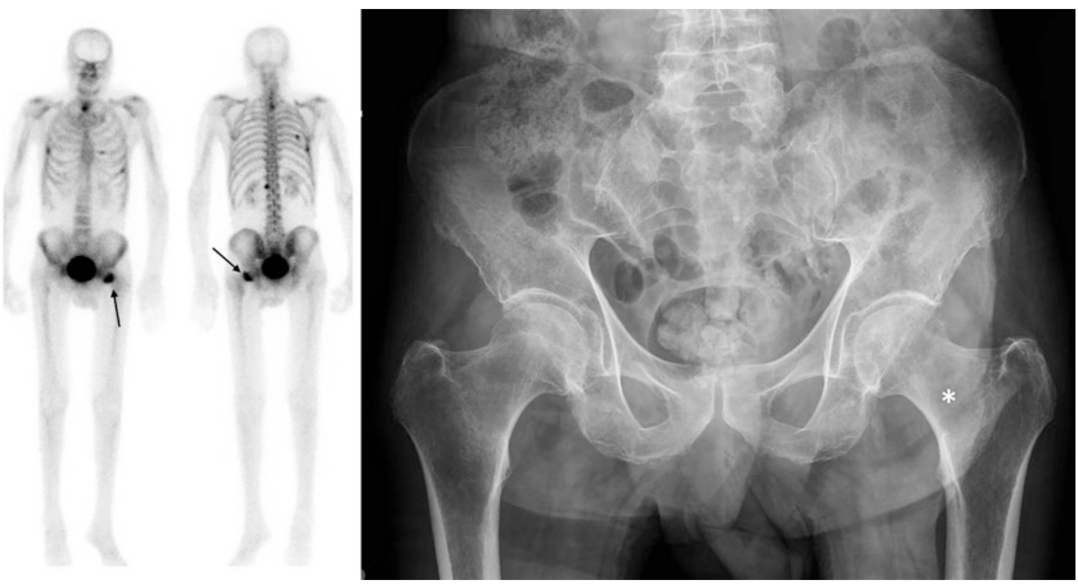

Fig. 3.8 The image on the left is a whole-body bone scan with anterior (left) and posterior (right) images showing a marked focus of increased uptake of the radiopharmaceutical in the left femoral neck (black arrows). Small foci overlying right ribs and the spine represent other metastases. The anteroposterior radiograph of the pelvis (right) shows a subtle lucency in the same position (asterisk). This represents a metastasis in a patient with a history of laryngeal squamous cell carcinoma

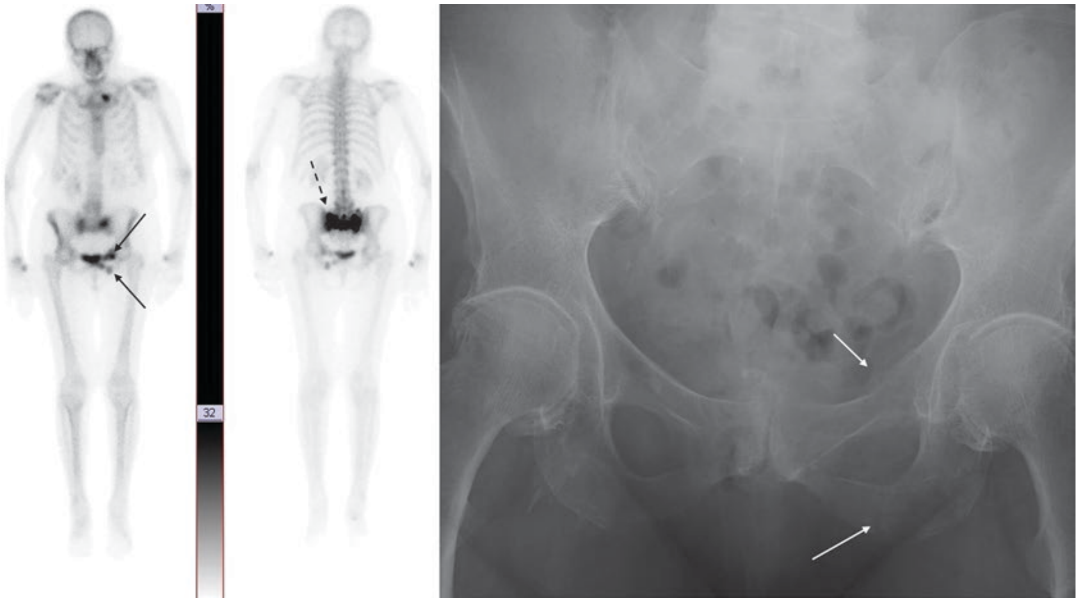

Fig. 3.9 Anterior and posterior images from a whole-body bone scan (left) show abnormal accumulation of the radiotracer in the sacrum (dashed black arrow) and in the left pubic rami (solid black arrows). The radiograph (right) shows healing insufficiency fractures in the left superior and inferior rami (white arrows). The associated sacral is not visible on the radiograph

over may accumulate the radiopharmaceutical and be seen on bone scanning. A fracture, for example, may continue to accumulate a bone-seeking radiopharmaceutical for many months after the fracture is clinically healed reflecting the long-term remodeling of the fracture. Joints affected by many arthritides may also accumulate abnormal amounts of the injected radiopharmaceutical and be seen on a bone scan. Soft tissue calcification and ossification also accumulate bone scanning agents (Fig. 3.11). In such cases, correlative imaging, often radiography or CT, may be needed for better definition of an abnormality detected on bone scanning.

While more sensitive than radiography in many cases, ^{99m}Tc bone scans have less spatial resolution than bone scans. Additionally, bone scanning may not be able to differentiate abnormal accumulation of the agent in bone from overlying foci of soft tissue uptake. The latter limitation can be lessened in fusion imaging in which the ^{99m}Tc bone scan is combined with CT scanning. In this case, the foci of abnormal accumulation of the radiopharmaceutical can be localized with correlative imaging (Fig. 3.12).

Positron emission tomography with computed tomography (PET/CT) is another example of fusion imaging. In this case, the radiopharmaceutical is often fluorine-18 deoxyglucose (^{18}F-FDG), a glucose analogue that enters the glycolysis pathway in metabolically active cells. Cancer cells typically are very glycolytically active and readily accumulate ^{18}F-FDG. Like ^{99m}Tc bone scans, ^{18}F-FDG scans alone are of limited spatial resolution, but combining the ^{18}F-FDG scanning with CT provides a precise anatomic localization of the accumulated radiopharmaceutical (Fig. 3.13).

3.4 Magnetic Resonance Imaging (MRI)

Unlike conventional radiography, CT and nuclear medicine, magnetic resonance imaging (MRI) does not rely on the use of ionizing radiation. Since MRI does not use ionizing radiation, MR scanning is associated with no known biologic hazard.

In MR imaging, the patient is placed into a gantry with a high-strength magnetic field, B_0,

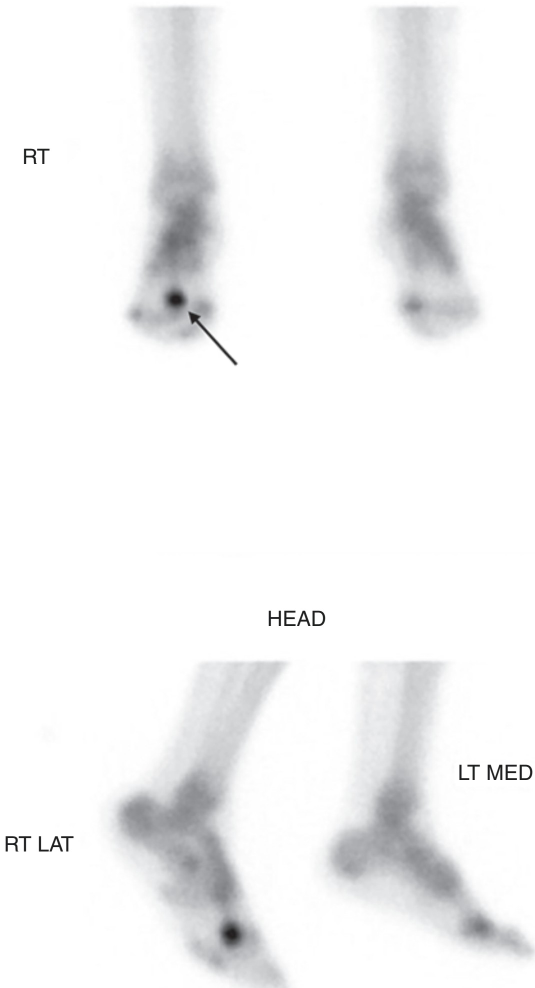

Fig. 3.10 Anterior and posterior whole-body bone scan images (left) show a marked focus of increased tracer accumulation in the forefoot (black arrow). Contemporaneous radiographs (not shown) were normal, but radiographs 2 weeks later reveal callus formation about the healing second metatarsal stress fracture (white arrow)

which causes the spins of the body's protons to align along the direction of B_0. During scanning, a magnetic field gradient is applied perpendicular to B_0, providing anatomic localization. Finally, a coil is used to apply a radiofrequency pulse of a predetermined frequency and at set intervals, called the *repetition time* (TR). The protons previously aligned along B_0 absorb a portion of the applied radiofrequency energy, and their axes of rotation displace from B_0 to some degree. The amount of displacement depends upon the duration and frequency of the radiofrequency pulse and the chemical environment of the population of protons being imaged.

After the cessation of the radiofrequency pulse, the protons precess back into alignment with B_0, releasing the absorbed radiofrequency energy. The length of time required for the protons to return to their baseline orientation in alignment with B_0 is known as *T1*. This process is often referred to as *T1 relaxation* or *spin-lattice relaxation*. As they return to the baseline, the spinning protons also release the absorbed energy as they lose their spin coherence and go

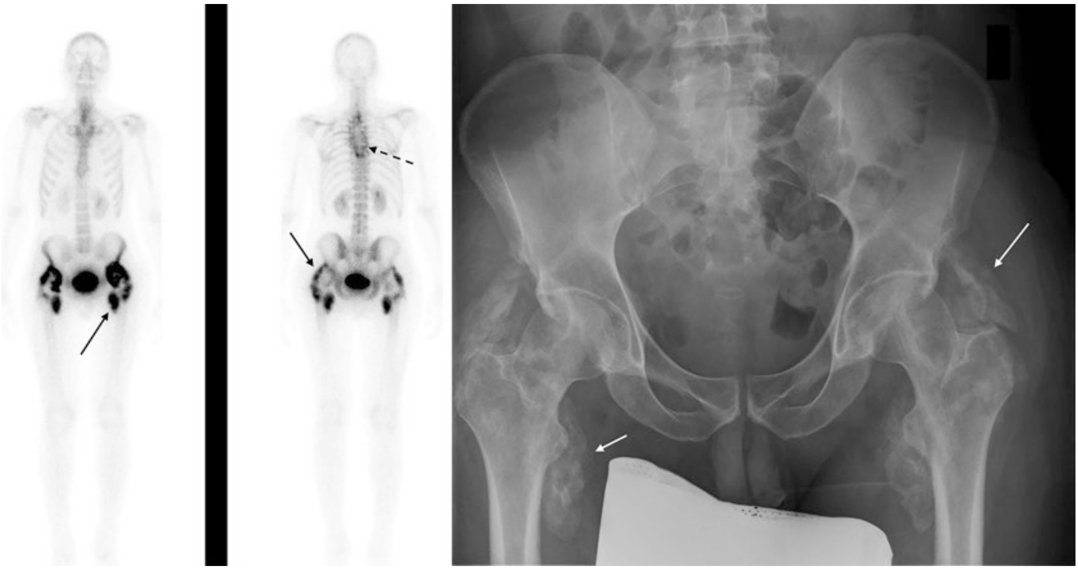

Fig. 3.11 Anterior and posterior bone scan images show intense foci tracer accumulation about both hips (black arrows). Accumulation of tracer over the upper thoracic spine (dashed black arrow) reflects spine surgery performed after a motor vehicle crash. The radiograph (right) reveals extensive heterotopic bone formation about both hips (white arrows)

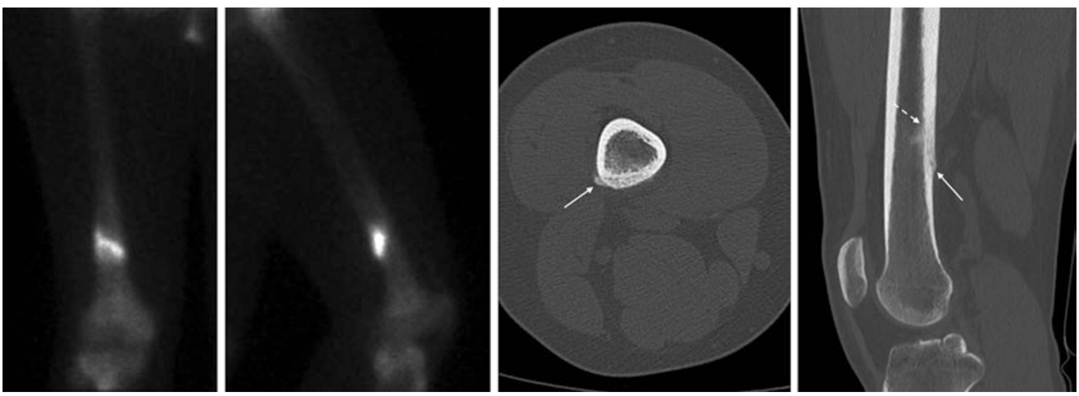

Fig. 3.12 Frontal and lateral bone scan images (left) demonstrate an intense focal of abnormal accumulation overlying the distal shaft of the femur posteriorly. Transverse and sagittal CT images (right) show immature callus formation and an incomplete cortical fracture along the posterior cortex of the femur (solid arrows) and sclerosis within the medullary canal of the femur (dashed arrow)

out of phase with respect to each other; this is referred to as *T2 relaxation* or *spin-spin relaxation*. The length of time required for the spinning population of protons to lose this coherence is known as *T2*.

The energy released by the protons as they return to the baseline alignment with B_0 is a combination of both T1 and T2 relaxation. The released energy is detected by the radiofrequency coil at set intervals following the initial pulse, often called the *echo time* (TE), and is the basis of the MR image. The rates at which the excited protons release the absorbed energy through T1 and T2 relaxation are determined by their molec-

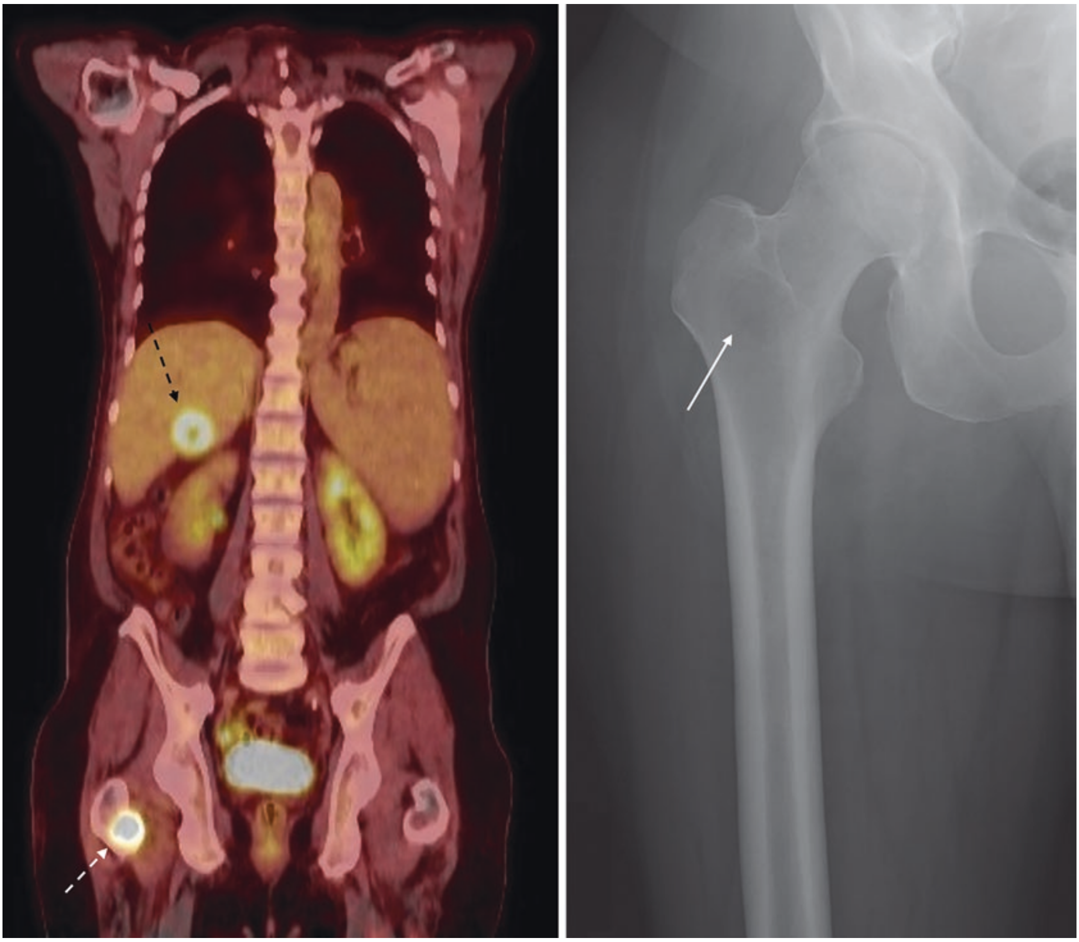

Fig. 3.13 A frontal PET/CT image of the body (left) in a patient with metastatic lung carcinoma shows an intense focus of abnormal accumulation of ^{18}F-FDG in the right femoral neck (dashed white arrow) and another lesion in the liver (dashed black arrow). A concurrent radiograph (right) demonstrates a lytic femoral neck metastasis (solid white arrow)

ular and tissue surroundings; that is to say that T1 and T2 vary by tissue type. By altering the time between radiofrequency pulses, TR, and the time at which the released energy is measured, TE, such tissue differences can be demonstrated on the MR image.

The specific TR and TE combinations and intervals used in the scan as well as the duration of the radiofrequency pulse make up a *pulse sequence*, and there is an enormous variety of clinically useful pulse sequences. Any MR image will show signals resulting from both T1 and T2 relaxation. A pulse sequence can be selected to emphasize differences in T1 between the tissues being imaged and results in a *T1-weighted image*. A different sequence can be used to emphasize differences in T2 between different tissues and produces a *T2-weighted image*. In a typical T1-weighted image, fat is bright, bone and fluid/water are dark, and muscle and soft tissues are intermediate to dark. T1-weighted images usually have good spatial resolution and are well-suited to showing structures and their relationship to fat or fat-containing structures (Fig. 3.14). A T2-weighted image typically displays water/fluid and fluid-containing tissues or structures as bright and fat and muscle as darker (Fig. 3.14). The high contrast between structures that do and

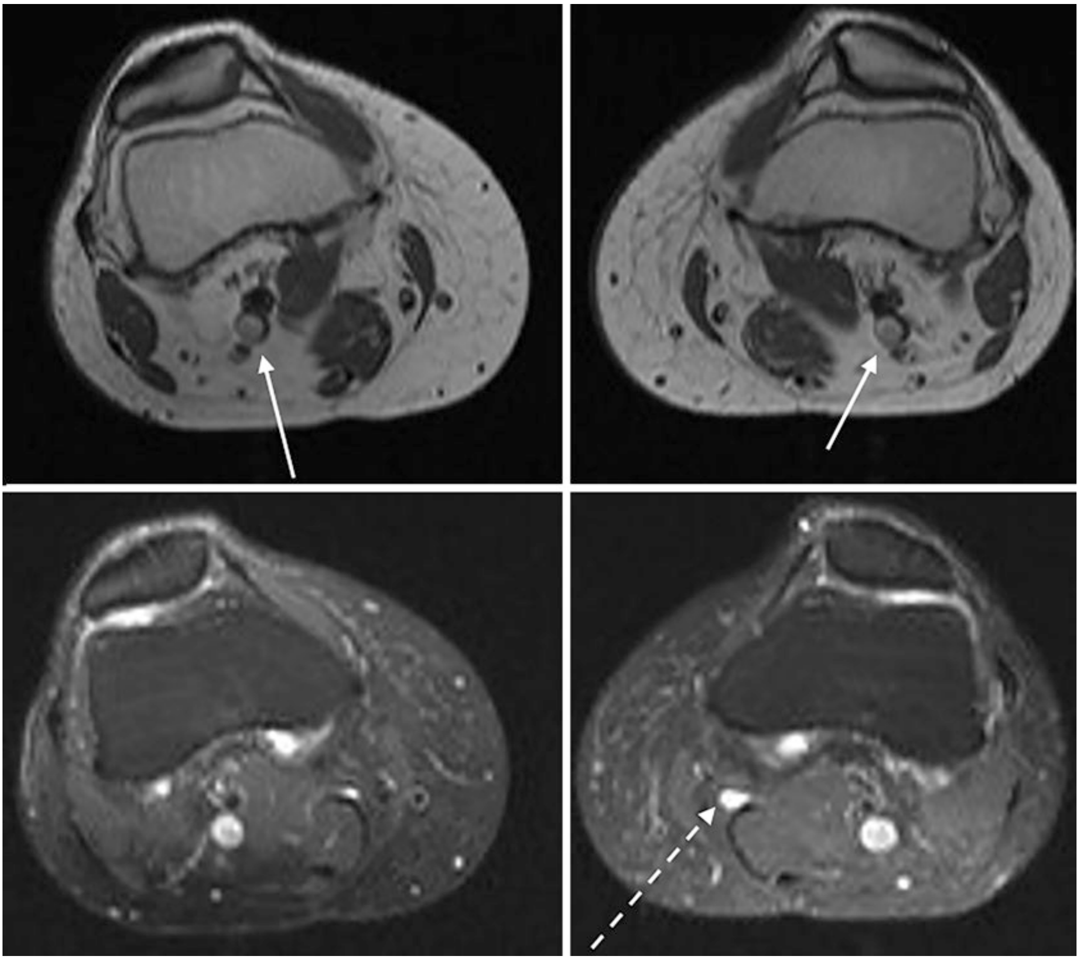

Fig. 3.14 T1-weighted transverse images at the level of the knees (top) show bright signal intensity arising from subcutaneous fat and from the marrow cavities. Note the sharp delineation of the neurovascular bundles (solid arrows) and various muscle bellies and tendon surrounded by fat. A T2-weighted image with fat suppression at the same level (bottom) has less contrast between fat and surrounding structures but demonstrates a small popliteal cyst on the left (dashed arrow) and a small amount of joint fluid between the patella and adjacent femur on both sides

do not contain water or fluid can be enhanced by selecting a pulse sequence that suppresses the signal arising from fat, an example of which is a fat-suppressed T2-weighted image (Fig. 3.15). A sequence that is commonly used in musculoskeletal imaging is the STIR (short tau inversion recovery or short T1 inversion recovery) sequence. The STIR sequence typically produces images with suppression of the fat signal (dark fat) and very bright water signal. Many other pulse sequences have been developed and can be used to answer a variety of clinical concerns.

These features of MRI make it ideal for imaging marrow-replacing processes such as osteonecrosis (Fig. 3.16) or marrow-infiltrating malignancies such as multiple myeloma (Fig. 3.17). These features also give MRI its ability to demonstrate the extent of soft tissue invasion and neurovascular involvement by neoplasms (Fig. 3.18). In some cases MRI can be highly suggestive of a histologic diagnosis when the lesion is seen to contain only homogeneous fluid (Fig. 3.19) or fat (Fig. 3.20). In other cases, however, the MR images may demonstrate a nonspecific mass with

Fig. 3.15 A sagittal fat-suppressed T2-weighted image of the knee shows a ruptured quadriceps tendon with associated edema and hemorrhage (*)

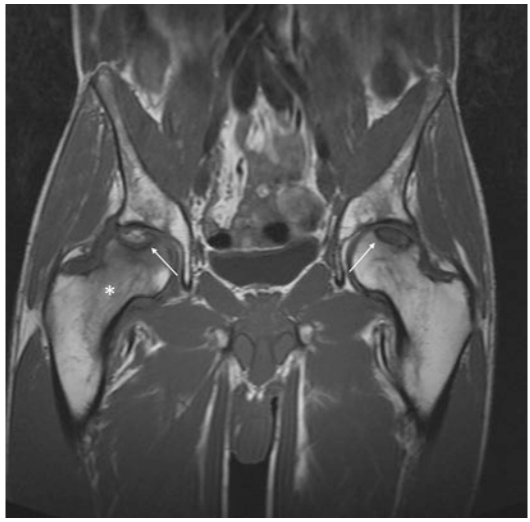

Fig. 3.16 A T1-weighted MR image of the pelvis demonstrates curvilinear foci of decreased signal intensity in both femoral heads (arrows) representing avascular necrosis. Decreased signal intensity in the right femoral neck (*) represents bone edema

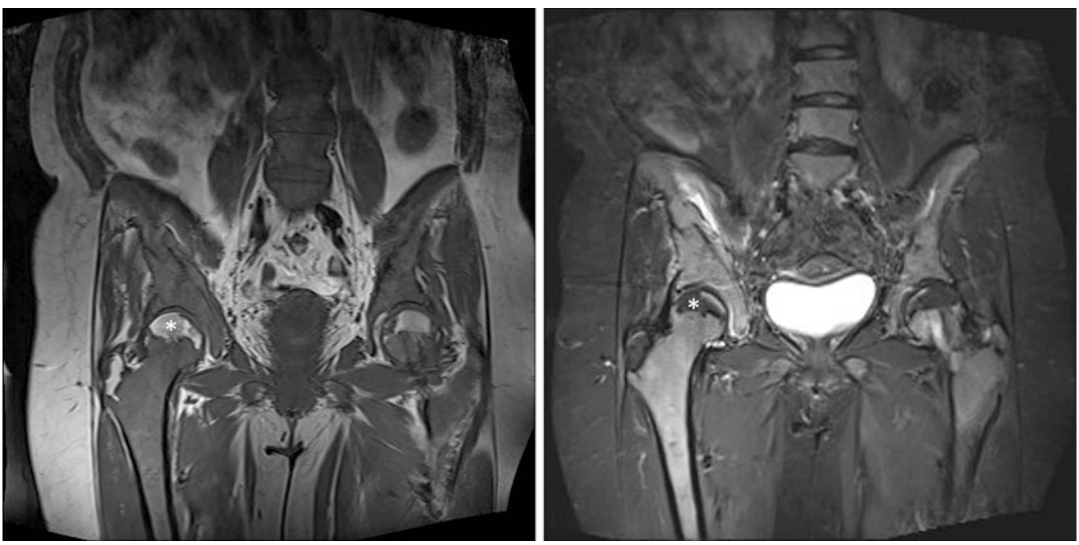

Fig. 3.17 T1-weighted (left) and fat-suppressed T2-weighted (right) MR images of a patient with multiple myeloma. The signal intensity in the femoral heads (*) is normal on both images. The bone marrow signal intensity throughout the remaining skeletal structures is diffusely low on the T1-weighted and high on the T2-weighted images indicating diffuse marrow infiltration by the malignancy

Fig. 3.18 Anteroposterior and lateral radiographs of the right proximal femur (left) show irregular periosteal new bone surrounding the shaft of the femur (solid arrows). A transverse fat-suppressed T2-weighted MR image through the proximal thigh shows a heterogeneous T2-intense mass (*) enveloping much of the femur and approaching the femoral artery (dashed arrow), identifiable by the pulsation artifact extending anterior and posterior to the artery

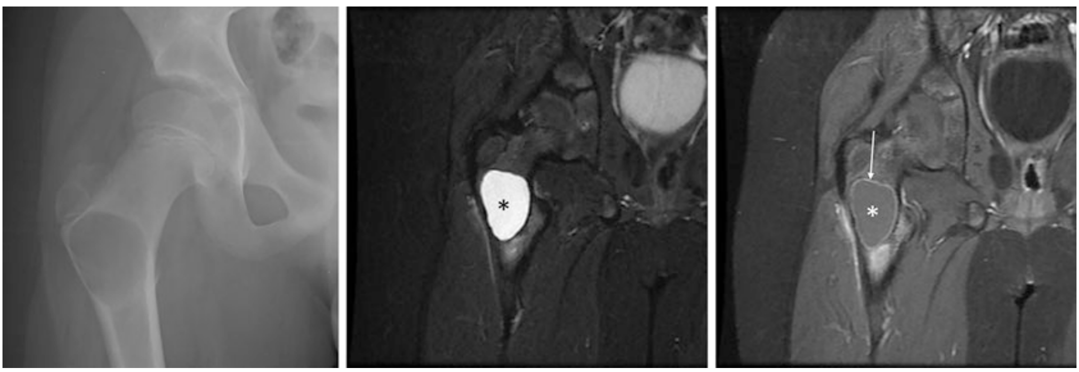

Fig. 3.19 An anteroposterior radiograph of the left hip (left) demonstrates a well-defined lytic lesion in the proximal femur centered at the level of the lesser trochanter, typical of a unicameral bone cyst. A coronal STIR image of the hip (center) shows a homogeneous hyperintense lesion (*) with a signal intensity indicating fluid. A T1-weighted fat-suppressed image after the administration of contrast (right) again shows decreased signal within the lesion (*) again indicating fluid but also shows mild enhancement of the inner lining of the lesion (arrow), further confirming its cystic nature

signal characteristics more comparable to muscle. Histologic diagnosis depends on biopsy in such cases (Fig. 3.21).

As suggested above, MR can be helpful in identifying causes of back and neck pain. Degeneration of an intervertebral disc with herniation of the nucleus pulposus is readily demonstrated on MRI (Fig. 3.22). MRI with sagittal and transverse imaging is also ideal in detecting spinal stenosis (Fig. 3.23).

Imaging of the internal structures at a joint is usually limited with conventional radiography, but MRI can readily demonstrate internal derangements such as meniscal tears and ligamen-

Fig. 3.20 A lateral radiograph of the hindfoot (left) reveals a well-defined lytic lesion in the mid calcaneus (*). On the T1-weighted MR image (center), the signal intensity in the lesion approximates that of marrow fat in the surrounding calcaneus, and on the STIR image (right), the signal intensity is low, again matching that of surrounding marrow fat in the calcaneus. These features confirm the diagnosis of intraosseous lipoma

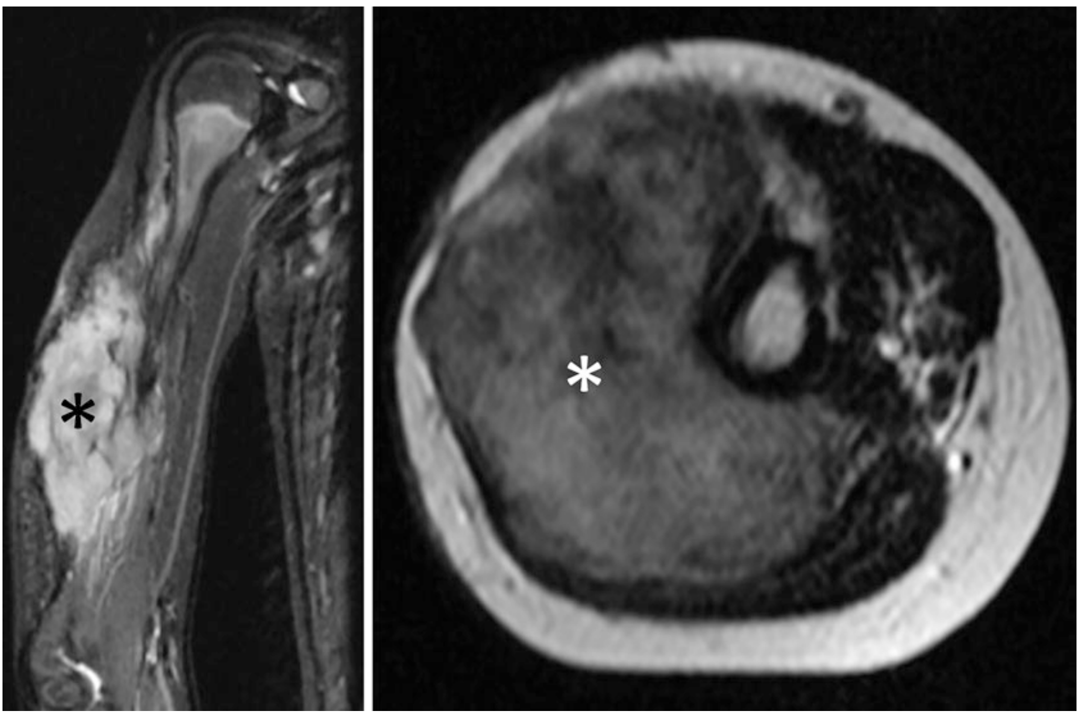

Fig. 3.21 Sagittal fat-suppressed T2-weighted (left) and transverse T1-weighted (right) images of the left arm show a large heterogeneous soft tissue mass encircling the humerus. The appearances are not specific, and biopsy is required to establish a histologic diagnosis, in this case fibromatosis

Fig. 3.22 A sagittal T1-weighted MR image of the lumbar spine demonstrates a large herniated nucleus pulposus (arrow) at the level of L5–S1

Fig. 3.23 A sagittal T1-weighted MR image of the cervical spine shows the spinal cord as a structure of intermediate signal intensity (*). Marked narrowing of the spinal canal results from discovertebral overgrowth anterior to the cord and hypertrophy of the ligamentum flavum posterior to the cord at the level of the C3–C4 intervertebral disc (arrows)

tous disruptions (Fig. 3.24). Rotator cuff tears at the shoulder (Fig. 3.25) and tendon and ligament injuries at the elbow (Fig. 3.26) are easily defined by MRI. Similar articular lesions can be demonstrated at other joints ranging from meniscal displacements at the temporomandibular joints to capsular tears at the metatarsophalangeal joints.

3.5 Ultrasound (US)

Compared to the previously discussed modalities, ultrasound (US) has a smaller role in musculoskeletal imaging. In US imaging, high-frequency sound waves are emitted by the US transducer in contact with the body part. The sound waves enter the body and are transmitted through tissues according to the tissue acoustic impedances, the abilities of the tissues to transmit sound waves. Tissue acoustic impedances vary greatly: water has a low impedance and transmits sound waves readily. Bone and air, on the other hand, have higher impedances and do not readily transmit the sound.

Having entered a tissue, the sound wave is reflected at interfaces between tissues of differing acoustic impedances. The sound wave might, for example, readily transit a fluid-filled structure such as popliteal cyst at the knee (Fig. 3.27). When the sound wave encounters the wall of the cyst, an interface between tissue of different acoustic impedances, an US echo is generated and detected by the transducer. The resulting image shows the wall of the cyst.

As suggested above, US is well-suited to the evaluation of fluid-filled structures such as

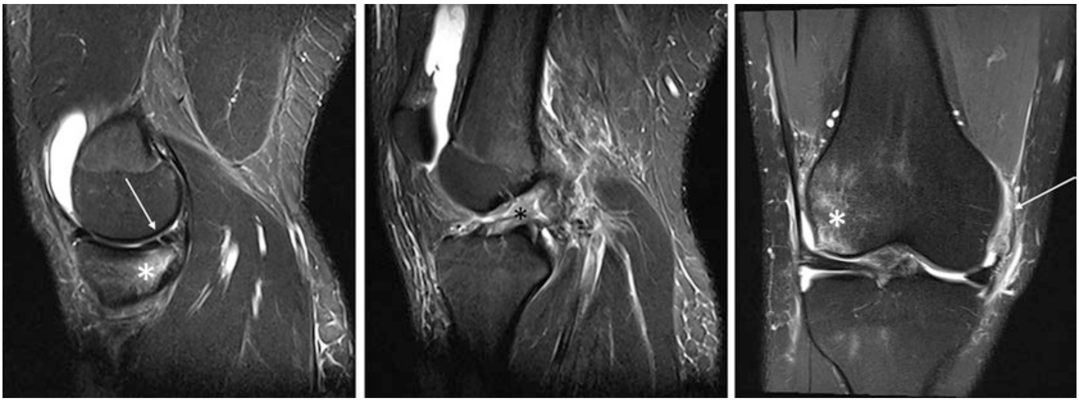

Fig. 3.24 Fat-suppressed T2-weighted MR images of knees. Bone contusions appear as foci of increased T2 intensity (white *). Sagittal images (left and center) demonstrate a tear of the posterior horn of the medial meniscus (arrow left) and of the anterior cruciate ligament (black * center). A coronal image (right) shows a tear of the medial collateral ligament (arrow)

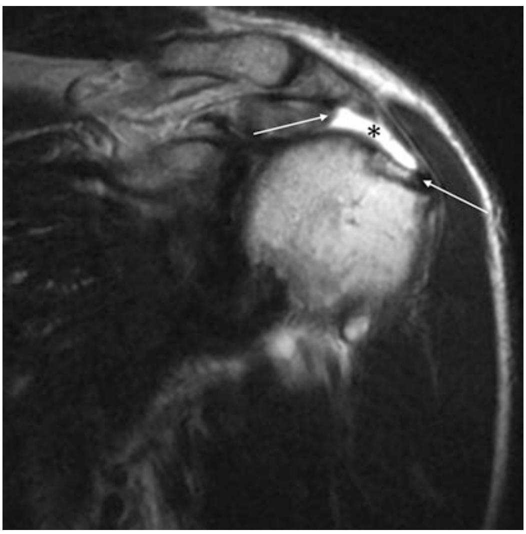

Fig. 3.25 A T2-weighted oblique coronal MR image of the shoulder shows joint fluid (*) interposed between the torn margin of the supraspinatus and its greater tuberosity insertion (arrows) indicating a full-thickness rotator cuff tear

cysts. Other soft tissue fluid collections such as abscesses and vascular lesions may be amenable to US imaging. The presence of a joint effusion can usually be established with US (Fig. 3.28). Tendons and ligaments can also be evaluated with US, but these examinations are time-consuming and require skilled examiners.

The evaluation of a solid soft tissue mass with US is generally nonspecific, although US-guided biopsy of a soft tissue mass may be appropriate as described below. The preoperative staging of a soft tissue mass is usually better performed with MRI, and US is generally not useful for the assessment of primarily osseous lesions.

3.6 Interventional Radiology

Articular imaging with MRI can be enhanced by the intra-articular administration of a contrast solution containing a diluted gadolinium-containing compound. These studies, MR arthrograms, can improve visualization of labral abnormalities at the hip or shoulder (Fig. 3.29). In other cases interosseous ligamentous injuries, at the wrist, for example, are better demonstrated by MR arthrography than by MRI alone (Fig. 3.30). In patients who cannot undergo MRI scanning, similar information can often be obtained by injection of the joint with diluted iodine-containing contrast followed by CT (Fig. 3.31).

Many joints can be aspirated or injected without imaging guidance. Small or difficult-to-enter

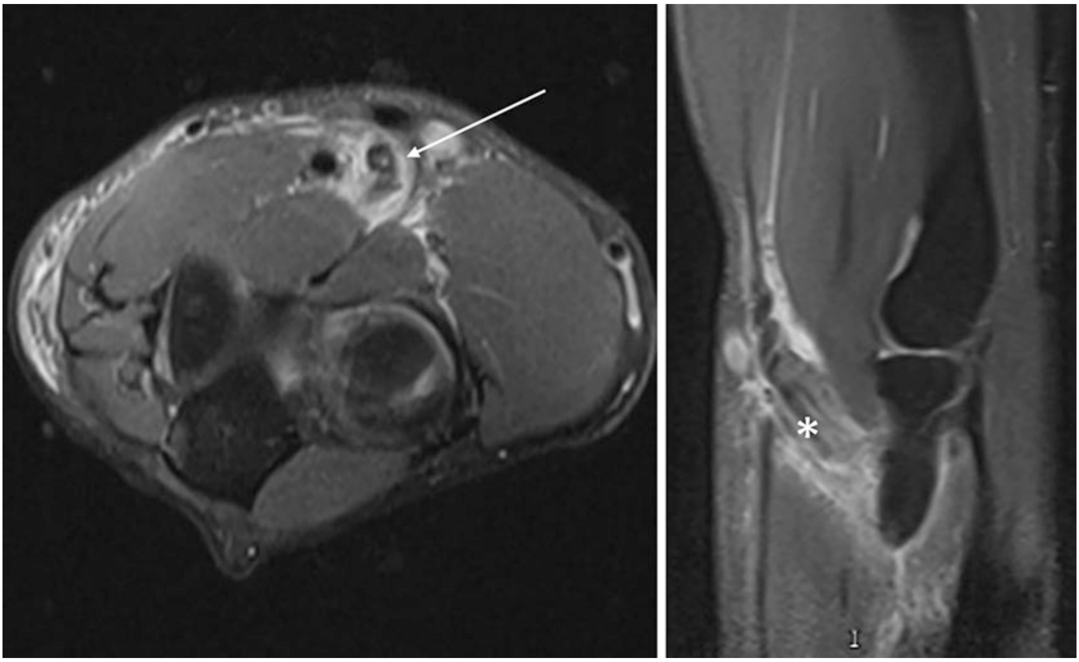

Fig. 3.26 Transverse (left) and sagittal (right) STIR images of the elbow reveal a complete tear of the distal biceps tendon (arrow and *) retracted proximally from its radial tuberosity insertion

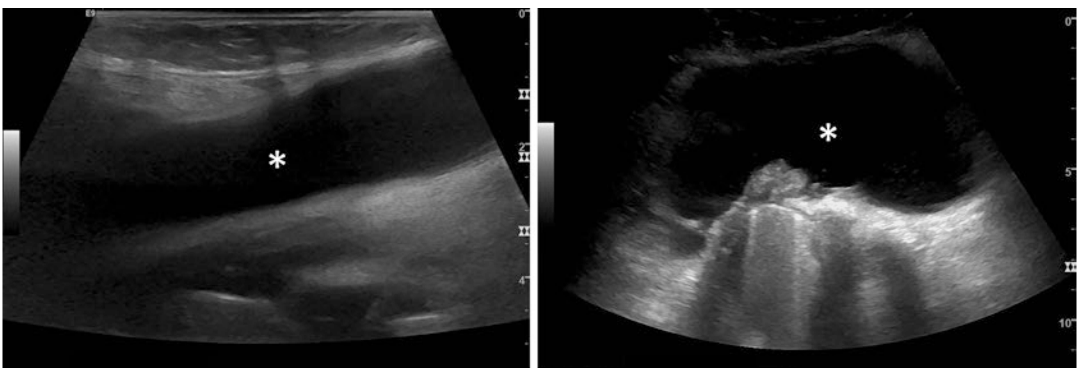

Fig. 3.27 Sagittal (left) and transverse (right) ultrasound images show a uniformly echo-free fluid collection (*) in the popliteal fossa, a typical popliteal cyst

joints, however, can usually be punctured with the guidance of fluoroscopy, US, or CT, and the correct intra-articular needle position can be confirmed with imaging after the injection of a small amount of contrast (Fig. 3.32).

Imaging-guided biopsy is appropriate for many musculoskeletal lesions such as primary and secondary neoplasms, metastatic disease to bone and soft tissue, and bone, soft tissue, and articular infection. CT, US, and fluoroscopy can all be used to guide a biopsy; the choice usually depends on the position of the lesion, the biopsy instrument to be used, and physician preference (Fig. 3.33).

Finally, certain musculoskeletal lesions may be definitively managed with imaging-guided

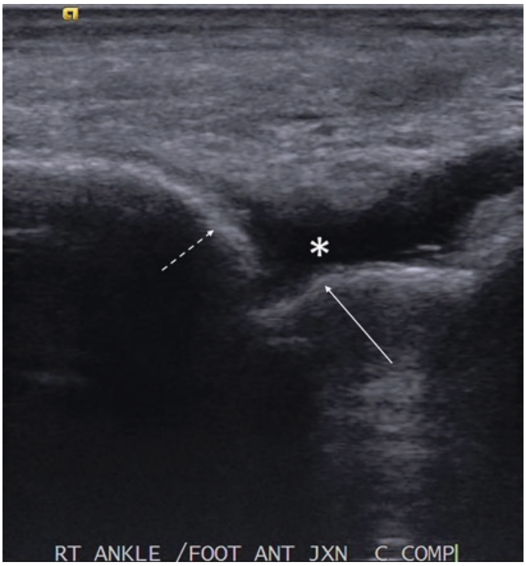

Fig. 3.28 An ultrasound image of the anterior surface of the ankle shows a tibiotalar effusion (*) and the adjacent surfaces of the tibia (dashed arrow) and talus (solid arrow)

Fig. 3.30 A coronal fat-suppressed T1-weighted image of the wrist after infection of gadolinium-containing contrast into the radiocarpal joint shows a tear of the scapholunate ligament (arrow) with contrast throughout the wrist joint compartments

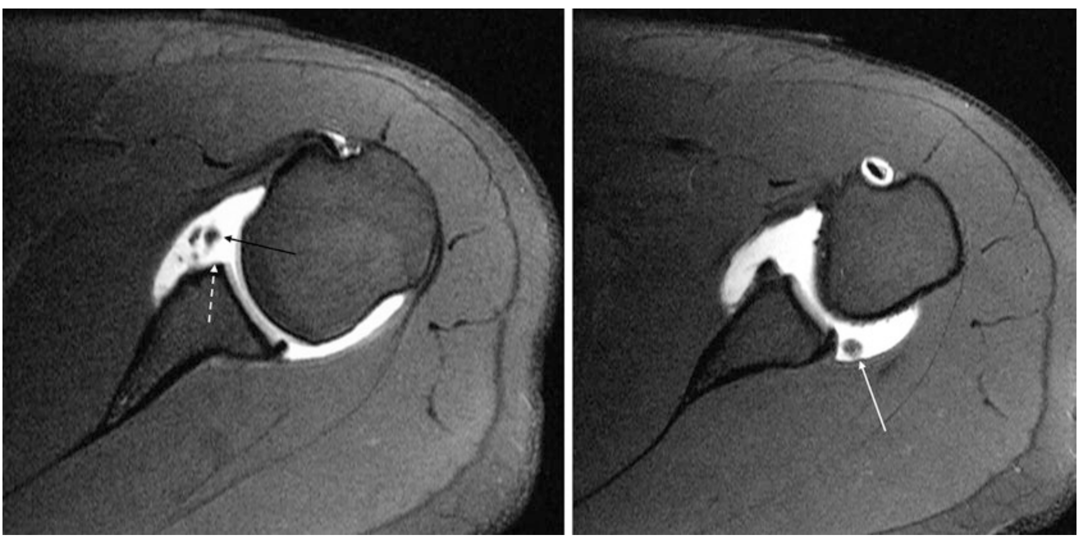

Fig. 3.29 Fat-suppressed T1-weighted transverse images of the shoulder obtained after the injection of gadolinium-containing contrast. The anterior glenoid labrum (black arrow) is torn and displaced anteriorly from its glenoid attachment site (dashed white arrow). There is an intra-articular loose body posteriorly (solid white arrow)

Fig. 3.31 Sagittal and coronal CT images of the left knee obtained after injection of iodinated contrast into the knee show contrast in the suprapatellar bursa (dashed arrow) and outlining the articular cartilage (solid arrows). The menisci (*) are surrounded by the contrast

Fig. 3.32 CT-guided injection of the posterior facet of the subtalar joint

interventions. Soft tissue vascular lesions such as hemangiomata can undergo successful embolization and aspiration. Osseous lesions such as aneurysmal bone cyst may sometimes be candidates for intralesional chemical ablation. Some metastatic lesions in bone can be treated palliatively with cryoablation, thermal ablation, and radiofrequency ablation. Osteoid osteomas can readily be ablated with radiofrequency ablation, typically under general anesthesia and with CT guidance (Fig. 3.34).

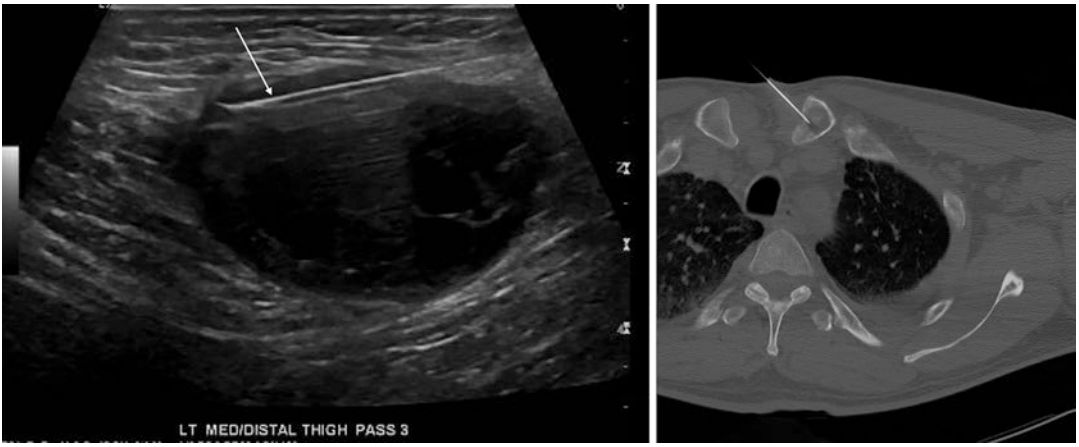

Fig. 3.33 Imaging-guided biopsies. On the left, ultrasound guidance is being used to biopsy a thigh mass, and the needle can be seen traversing the mass (arrow). On the right, a destructive lesion in the medial left clavicle is being biopsied with CT guidance

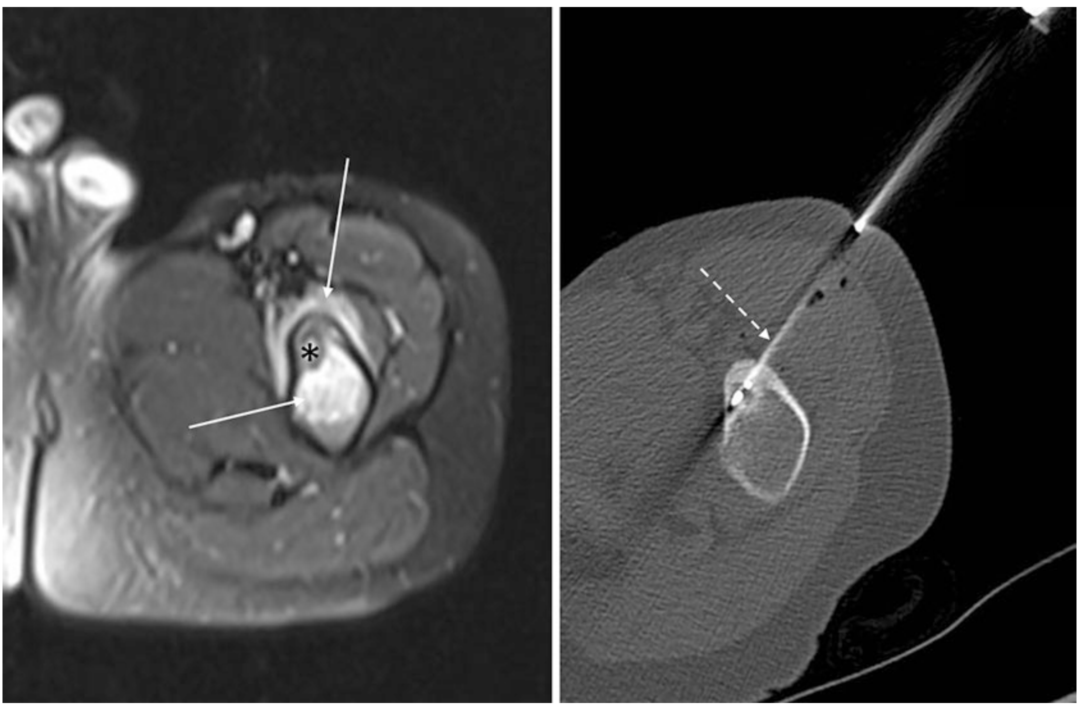

Fig. 3.34 Osteoid osteoma ablation. A T2-weighted MR image of the proximal femur (left) shows the nidus of an osteoid osteoma (*) and surrounding bone and soft tissue edema (arrows). Under CT guidance (right), a radiofrequency probe (dashed arrow) is placed into the nidus and an ablation is performed

3.7 Summary

An array of modalities is available for the imaging of the patient with a musculoskeletal condition. Conventional radiography, CT, nuclear medicine, US, MRI, and interventional radiology may all be employed in the evaluation and treatment of a variety of diseases and processes, although imaging usually begins with the use of conventional radiography. The prudent selection of further imaging modalities will help result in efficient and cost-effective imaging with the least risk to the patient.

Basic Bone Metabolism

4

Meghana Bhatta and Morgan S. Jones

Contents

Goals and Objectives

- *Goal*: To present the basic concepts of bone formation and resorption and the factors that govern bone development to lay the physiologic groundwork to understand bone disorders
- *Objective*: On the completion of this unit, the learner should be able to describe, list, or identify:
  1. The four purposes of the skeletal system
  2. Bone transformations through various life stages
  3. Structure and composition of long bones
  4. Three major cells involved in the bone remodeling cycle and their respective roles
  5. Signaling pathway for osteoclast activation

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6. Hormones that regulate calcium and phosphate balance and bone remodeling
7. Laboratory measures that reflect status of bone turnover

4.1 Introduction

The skeleton is a complex organ that has multiple functions. It provides structure and protection to the body. Bones also have many other functions. Prior to describing these functions, it is important to review important definitions. In the next section, these definitions will be reviewed. This chapter will then outline the basics of bone metabolism and function to lay the foundation for understanding medical bone disorders.

4.2 Important Definitions

Epiphysis The two rounded ends of a long bone, separated by a shaft.

Diaphysis The shaft or midsection of a long bone, flanked by the epiphysis on both ends.

Metaphysis A portion of long bone that separates the epiphysis and diaphysis. It contains the epiphyseal growth plate, which is made of cartilage and grows during childhood.

Cortical (compact) bone A type of bone that is dense, making it resistant to stress and trauma. It forms the protective outer layer of bones.

Trabecular (spongy, cancellous) bone A type of bone that is porous with a honeycomb-like structure. It comprises the epiphyses of long bones.

Periosteum A dense layer of connective tissue that surrounds the exterior of bones. It contains cells that help regenerate bone after trauma.

Endosteum A layer of connective tissue that lines the central cavity of long bones, which holds bone marrow.

Woven bone A weak early form of bone that is made of irregularly arranged collagen fibers. It is present in the embryonic skeleton and is in states of rapid bone changes.

Lamellar bone Mature, mechanically strong bone characterized by collagen fibers laid in an orderly fashion.

Osteons (Haversian system) The basic structural unit of compact bone, consisting of concentric layers of bone surrounding a central vascular canal. They measure several millimeters long and 0.2 mm in diameter.

Bone resorption The process in which bone tissue is broken down, and minerals are released into the bloodstream.

Bone formation The process in which new bone material is created and deposited.

Osteoclasts Cells that cause bone resorption by secreting enzymes to dissolve bone tissue.

Osteoblasts Cells that cause bone formation by synthesizing and mineralizing bone matrix.

Osteocytes Quiescent osteoblasts trapped in the bone matrix. They participate in maintenance of the bone matrix and direct bone metabolism.

Basic multicellular unit (BMU) A term to describe the basic unit of bone remodeling. It includes the osteocyte, osteoclast, and osteoblast.

Bone mineral density (BMD) A measure of bone mineral architecture and strength that has been correlated with fracture risk. It is often referred to as bone density.

Low trauma fracture (fragility fracture) There is not a single definition for low trauma fractures. The general definition is a fracture in a person from low or no trauma that would not lead to a fracture in a patient with healthy bones. They typically affect the hips, spine, and wrist. Examples include femoral neck or wrist fractures

after a fall from a standing height or compression fractures of the spine with no known trauma. Low trauma fracture, fragility fracture, and major osteoporotic fracture are used interchangeably in this chapter.

Dual-energy X-ray absorptiometry (DXA) An imaging modality using X-ray to calculate an estimate of BMD. Typically, the BMD of the lumbar spine, total femur, and femoral neck is measured. The forearm and other areas are calculated in special clinical situations.

4.3 Overview of the Skeletal System

4.3.1 Purposes

The skeleton system is a complex network of bones and cartilage that forms the scaffolding for the human body. Bones maintain the structural integrity of the body and provide protection for vital internal organs. Movement is facilitated via contraction of muscles attached to jointed bones. Hematopoiesis occurs inside red bone marrow and fat is stored in yellow bone marrow. Finally, the skeleton serves as a reservoir of minerals and is crucial for regulation of calcium, phosphate, and acid-base balance [1].

4.3.2 Structure

The adult skeleton contains 213 bones. Bones may be classified into five categories based on shape. These include long bones, short bones, flat bones, sesamoid bones, and irregular bones (Table 4.1). Long bone is formed by rounded epiphysis at the two distal ends and the diaphysis in between. A metaphysis separates the epiphysis and diaphysis and contains the epiphyseal plate. This is made of cartilage and grows throughout childhood. In early adulthood, the epiphyseal plate is replaced by osseous tissue, which leads to the cessation of growth (Fig. 4.1).

Cortical, or compact, bone is dense and strong. This is the type of bone that makes up the diaphysis. Inside the diaphysis is the medullary capillary which stores yellow bone marrow. The surface of the bone is covered by the periosteum, which provides nutrition to the bone. Sharpey's fibers adhere the periosteum to the cortical bone.

Table 4.1 Types of bones, where they are located and their purpose

Type of bone	Purpose	Examples
Short	Facilitate movement and provide stability	Wrists, ankles
Long	Facilitate movement and support weight	Upper and lower extremities
Flat	Protect internal organs	Skull, thoracic cage, pelvis
Sesamoid	Protect internal organs	Vertebral column, pelvis
Irregular	Protect tendons	Kneecap

Trabecular bone is more porous and has a higher rate of turnover than cortical bone. It is also called spongy or cancellous bone. The epiphysis is comprised of trabecular bone. Red marrow is stored inside the epiphysis, which is where hematopoiesis occurs.

Woven bone is an immature form of bone. It can be either cortical or trabecular bone. Collagen fibrils, which are basic building blocks of bone, are laid down in a disorganized pattern in woven bone. This type of bone is formed during development and immediately after a fracture during repair. In diseases with rapid bone turnover, there is often excess woven bone. Lamellar bone eventually replaces woven bone. Lamellar bone is a more mature bone in which collagen is deposited in an orderly fashion.

The basic structural unit of the bone is called an osteon. Osteons consist of concentric layers of osseous tissue that surround a central canal. Inside the canal is a blood vessel, which supplies the osteon (Fig. 4.2).

Bone is a rigid connective tissue that is comprised of organic and inorganic compounds. The organic matrix is comprised of collagen fibers and ground substance. Ground substance consists of extracellular fluid and proteoglycans. The organic matrix confers elasticity to the bone. Inorganic salt crystals confer hardness and strength to the bone. These inorganic salts are

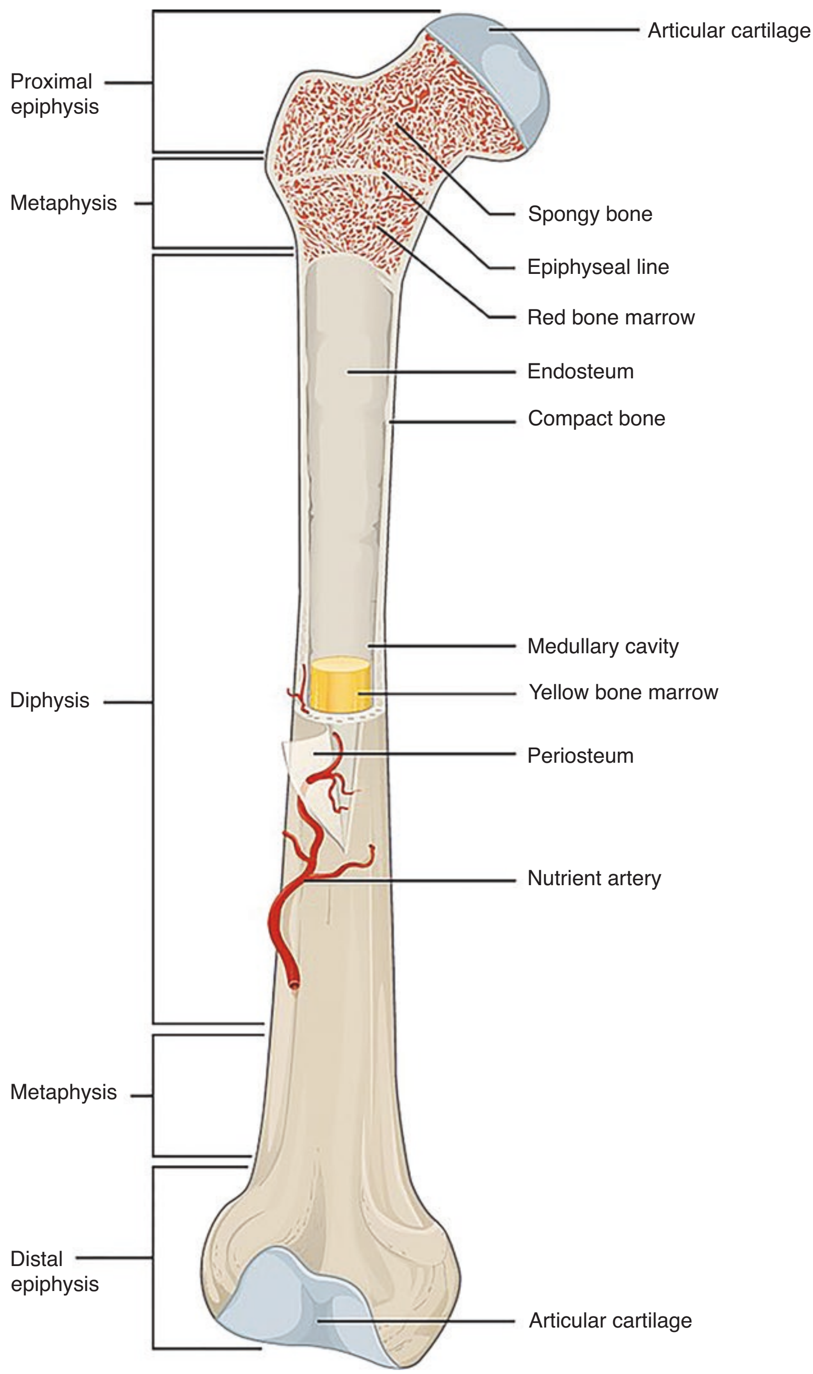


Fig. 4.1 Basic anatomy of the bone. (From https://commons.wikimedia.org/wiki/File:603_Anatomy_of_Long_Bone.jpg)

primarily comprised of hydroxyapatite which is a calcium and phosphate salt. Carbonate, magnesium, and acid phosphate are also present in the bone in smaller quantities. Compact bone has a greater proportion of inorganic salt crystals compared to other types of bone [2]. The tightly coordinated network of collagen and salt crystals is integral for making bone rigid yet flexible. This grants bone the ability to withstand loads without breaking.

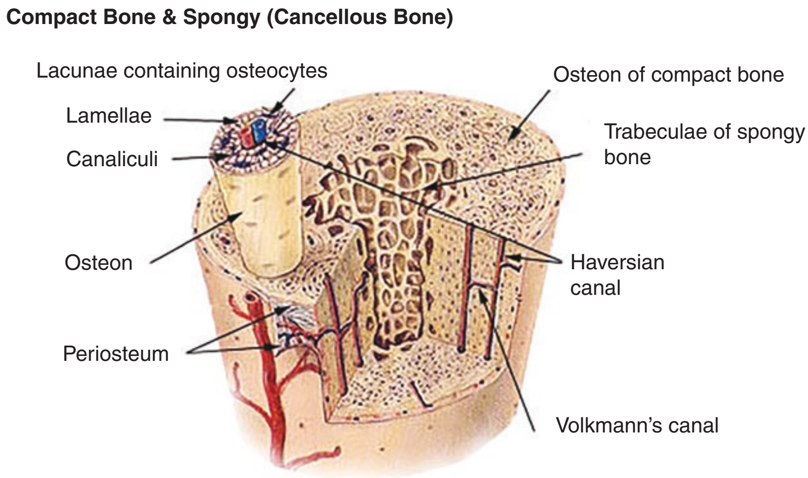


Fig. 4.2 The basic structural unit of the bone. (From https://en.wikipedia.org/wiki/Osteon#/media/File:Illu_compact_spongy_bone.jpg)

4.3.3 Bone Remodeling

Bone is a dynamic organ. It is constantly adapting to new mechanical demands and renewing itself. During childhood and adolescence, bone undergoes longitudinal and radial growth. This is driven primarily by cartilage growth at the epiphyseal plates of the long bones. Eventually, the cartilage is mineralized into bone, and the epiphyseal plates close. When the plates close, people have peak bone mass. This typically happens when people are around 25 years old. Bone remodeling is in balance for 5 years after peak bone mass is achieved. Around the age of 30 years, people begin to lose bone mass. During this time, bone resorption exceeds the rate of bone formation, and people lose approximately 0.5% of their bone mass per year. Bone loss accelerates at a greater rate in women after menopause [2–4].

Bone remodeling primarily serves to repair microtraumas. This helps to adapt to new stressors and renew old, weak bone. Four phases define the bone remodeling cycle. First, there is a stimulus to start bone remodeling. Second, resorption or breakdown of bone occurs. Next, there is a transition from resorption to bone formation. Lastly, new bone is generated, completing the cycle. Nidi of bone remodeling occur at random sites throughout the bone. Bone resorption usually takes 2–4 weeks to complete, whereas bone formation takes 4–6 months to complete. The bone balance represents the difference between resorbed and formed bones (Fig. 4.3). Excess resorption caused by certain diseases or medications can lead to an imbalance of bone metabolism and low trauma fractures.

Osteoblasts, osteoclasts, and osteocytes are the key cells that participate in bone remodeling. These are sometimes referred to as the basic multicellular units (BMU). Osteoclasts are derived from monocytes and macrophages from the bone marrow. Osteoblasts originate from osteogenic cells that originate deep within the periosteum and bone marrow [5]. Osteocytes are derived from osteoblasts. They are formed when an osteoblast becomes embedded in the bone matrix.

New bone is formed by osteoblasts. Osteoblasts synthesize collagenous matrix and enact mineralization of the matrix. Osteoid is made around the osteoblasts, and the matrix is then calcified. When this happens, a minority of osteoblasts are retained in the mineralized space. These spaces are called lacuna. Osteoblasts trapped in this space transform into osteocytes. The osteocytes act as mechanoreceptors that regulate bone metabolism based on environmental stressors. Some osteoblasts remain at the bone surface where they can be activated if exposed to stimuli. The remainder of the osteoblasts undergo apoptosis [4].

Osteoclasts are responsible for bone digestion via the secretion of proteolytic enzymes and acids. Receptor activator of nuclear factor-kappa B (RANK) and macrophage colony-stimulating

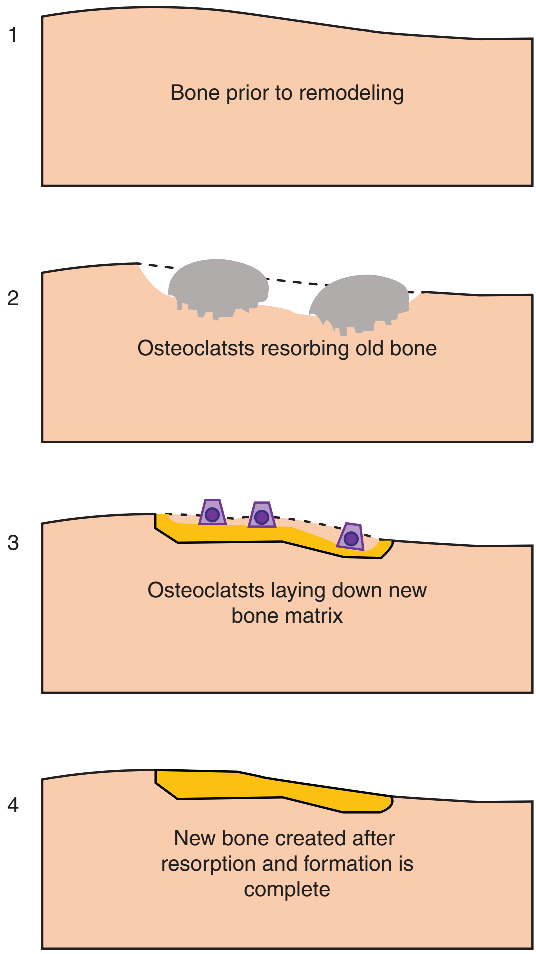


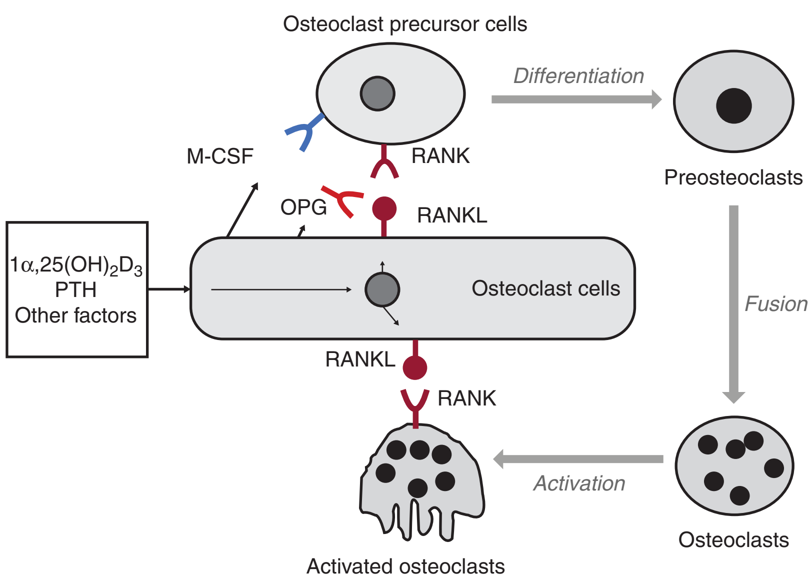
Fig. 4.3 The steps of basic bone remodeling

factor (M-CSF) are two cytokines produced in the bone marrow and osteoblasts. RANK and M-CSF recruit osteoclasts from the circulation and stimulate osteoclast proliferation and differentiation. RANK ligand (RANKL) binds to RANK on osteoclast precursors leading to their activation. Problems with this pathway can cause disorders of bone resorption. Excess RANKL causes an imbalance of bone resorption compared to bone formation and leads to low bone density and low trauma fractures. This molecular pathway is the target of some osteoporosis treatments including denosumab. Osteoprotegerin (OPG), which is an osteogenesis-inhibitory factor, is a decoy receptor important for bone remodeling. RANKL binds to this receptor to inhibit osteoclast formation and inhibit bone resorption [6, 7]. Figure 4.4 outlines the RANK and RANKL pathway.

4.4 Regulation of Bone Development

A number of hormones in the body affect bone development. Some favor bone resorption and others favor bone formation. When absorption and formation are in balance, multiple factors affect the bone and are regulated by complex feedback systems. Calcium and phosphorus are essential to the formation of bone. Factors that

Fig. 4.4 Osteoclast differentiation by the RANK-RANKL pathway



affect their balance (Table 4.2) affect overall bone structure and function.

4.4.1 Hormones That Affect Calcium and Phosphate Homeostasis

Vitamin D Vitamin D_3 (cholecalciferol) is synthesized in the skin through sun exposure. Vitamin D_3 and vitamin D_2 (ergocalciferol) are also absorbed through the gastrointestinal (GI) tract from certain plants and other foods in the diet. Cholecalciferol and ergocalciferol are hydroxylated in the liver to form 25-hydroxyvitamin D (calcidiol). Calcidiol is then hydroxylated in the kidneys to make 1,25-hydroxyvitamin D (calcitriol). Calcitriol is the most active form of vitamin D. Vitamin D receptors are ubiquitous in the body. Calcitriol promotes calcium and phosphate absorption through the intestinal epithelium. It also inhibits excretion of these minerals through the urine. Overall, vitamin D promotes healthy growth and remodeling of bone. Vitamin D activation and uptake is subject to positive and negative feedback regulation. Severe vitamin D deficiency causes osteomalacia, rickets, and low trauma fractures. Figure 4.5 outlines vitamin D metabolism and action.

Table 4.2 Factors that affect calcium and phosphate regulation

	Serum calcium	Serum phosphorus
PTH	↑	↓
Calcitriol	↑	↑
Calcitonin	↓	↓
FGF-23	–	↓

Parathyroid Hormone (PTH) There are four parathyroid glands in the typical human that are located posterior to the thyroid gland in the neck. PTH has a rapid and potent effect of mobilizing calcium from the bone and decreasing renal excretion of calcium. It also causes phosphate absorption from the bone and increases phosphate excretion through the kidneys. Chronic exposure to PTH causes excess bone resorption by activating osteoclasts through the RANK-RANKL pathway [8]. Conditions such as primary hyperparathyroidism that cause prolonged exposure to high PTH levels are associated with

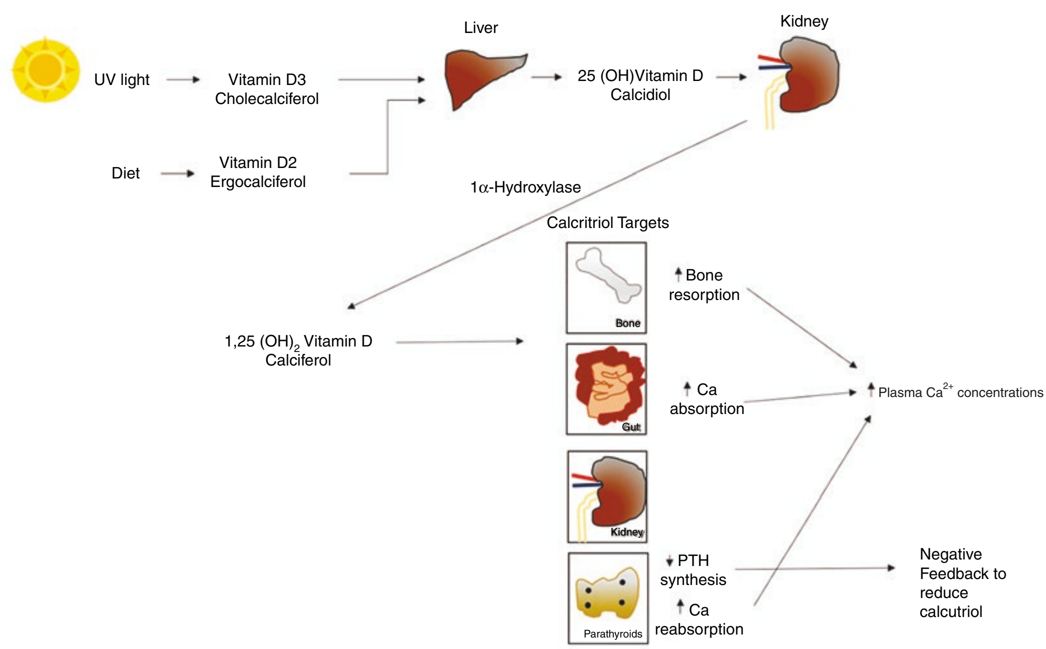


Fig. 4.5 Vitamin D synthesis

low trauma fractures and osteoporosis. In a healthy body, however, PTH helps regulate healthy bone metabolism. Interestingly, intermittent exposure to PTH analogs favors bone formation. This has led to the use of PTH analogs such as teriparatide in the treatment of osteoporosis.

Calcitonin Calcitonin is produced by C-cells in the thyroid gland. It downregulates calcium release from the bone and calcium reabsorption from the kidneys. It effectively antagonizes the effects of PTH. The effects of calcitonin are comparatively weak and short-lived compared to the effects of PTH however.

Fibroblast Growth Factor 23 (FGF-23) FGF-23 is a phosphaturic hormone produced by osteocytes. Its function is not entirely clear. Excess FGF-23 leads to increased renal tubular phosphate reabsorption and an overall increase in secretion of phosphate through the urine. This leads to decreased serum phosphate levels and weak bones prone to low trauma fractures. Elevated FGF-23 is seen in genetic cases of rickets and osteomalacia and in patients with chronic kidney disease [9]. Although the exact mechanism is unclear, it appears FGF-23 is a major factor in phosphate regulation and many bone pathologies.

4.4.2 Hormones That Affect Bone Resorption

Sex Hormones Androgens and estrogens mediate longitudinal and radial bone growth during adolescence by stimulating osteoblast differentiation. They also regulate osteoclast activity. In addition, androgens increase muscle mass, which provides greater mechanical stress on bones and further increases osteogenesis.

Glucocorticoids Glucocorticoids affect bone through the RANK-RANKL/OPG pathway. They stimulate RANKL, which leads to excess osteoclast activity and increased bone resorption [10]. They also inhibit sex hormone production, which has a negative effect on the bone. Finally, they interfere with osteoblast recruitment and cause osteocyte apoptosis. Excess glucocorticoid activity from Cushing's disease or syndrome as well as iatrogenic Cushing's caused by glucocorticoid therapy may lead to severe bone disease. Profound bone loss can occur within months of starting glucocorticoid therapy. Rapid decline in bone mass can occur and lead to low trauma fractures.

Insulin There is emerging evidence that insulin has an anabolic effect on bone. This occurs via stimulation of osteoblast differentiation, which leads to increased bone formation. It is unclear what role this may play in patients with insulin resistance conditions such as type 2 diabetes [11]. Patients with diabetes mellitus are at increased risk for osteoporosis.

Thyroid Hormone Thyroid hormone promotes bone resorption. Excess thyroid hormone, seen in patients with hyperthyroidism, leads to low bone density and an increased risk for fracture.

4.5 Measures of Bone Quality and Turnover

4.5.1 Imaging

When patients are evaluated for fractures, the first step is typically an X-ray. For patients at risk for osteoporosis or low bone density, the best image is a DXA. DXA is the preferred mode of measuring bone density for surveillance and for predicting fracture risk. It utilizes the absorption of radiation in bone over a given surface area to estimate BMD. Typical areas measured include central areas such as the lumbar spine and hip along with peripheral areas such as the radius, heel, and hands. By convention, a standard DXA measures bone density at the lumbar spine, femoral head, and femoral neck. Peripheral areas, specifically the distal one-third of the radius, are measured in certain clinical situations, the most common being hyperparathyroidism. In a standard DXA, the absolute BMD is reported. The T-score represents a comparison of the patient's bone density

compared to a young, healthy female population at maximal BMD. This is applied to postmenopausal women and men over the age of 60 for the diagnosis of osteoporosis. For premenopausal women and younger men, a Z-score is used to evaluate bone density. Z-score provides a comparison of bone density compared to an age- and gender-matched database [12, 13].

4.5.2 Biochemical Markers for Bone Turnover

There are several bone turnover markers that can be used to assess bone metabolism. Urinary N-telopeptide cross-link (NTX) and serum C-telopeptide cross-link (CTX) are peptides released during bone resorption. They can be measured by commercial labs and may have some clinical utility to evaluate osteoporosis treatment effectiveness [14, 15]. However, these labs are generally not used as it is unclear what clinical impact these monitoring labs have for patients.

Alkaline phosphatase and N-terminal propeptide of type I procollagen (PINP) are by-products of osteoid formation. These are markers of bone formation. They can also be used to monitor therapy in patients with osteoporosis [14, 15], although their overall utility is questionable. In patients with Paget's disease, alkaline phosphatase is an essential marker of bone formation that should be monitored during therapy and is used for diagnosis as well.

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5

Principles of Diagnosis and Treatment of Bone Remodeling Disorders

Roger Harty and Morgan S. Jones

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the diagnosis and treatment of bone remodeling disorders with an emphasis on Paget's disease of the bone
- *Objective*: On completion of this unit, the learner should be able to describe, list, or identify:
  1. The diagnostic workup of bone remodeling disorders
  2. Different causes of bone remodeling disorders
  3. Clinical manifestations of Paget's disease of the bone

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4. Radiographic findings of Paget's disease of the bone
5. Hallmarks of treatment for Paget's disease of the bone

5.1 Diagnosis of Bone Remodeling Disorders

Bone is constantly being remodeled to ensure development and maintenance of a healthy skeletal system. Normal bone remodeling is dependent upon several factors. Bone remodeling is under the auspices of osteoclasts which cause bone resorption, and osteoblasts which stimulate bone formation. This interplay between osteoclasts and osteoblasts is under a system of checks and balances through a complex signaling cascade that ensures healthy bone formation. Disruption of this signaling cascade can lead to abnormal bone remodeling and ultimately result in diseased bones. This can occur in a variety of manners that will be elaborated on in this chapter.

5.1.1 Common Disorders of Bone Remodeling

There are several disorders of bone remodeling including but not limited to osteoporosis, chronic kidney disease-mineral and bone disorder (CKD-MBD), Paget's disease of the bone, and osteopetrosis [1]. These diseases are outlined in Table 5.1. This chapter will focus on Paget's disease of the bone and other disorders of bone remodeling outside of osteoporosis. Osteoporosis will be reviewed briefly in this chapter and has an entire chapter devoted to it as well.

5.1.1.1 Osteoporosis

Osteoporosis is the most common disorder of bone remodeling. Osteoporosis is associated with low bone mass and disruption of the normal remodeling of bone. This leads to increased bone fragility and predisposes an individual to fracture. There are a variety of mechanisms that can lead to the development of osteoporosis through disruption of normal remodeling. Some of these processes include postmenopausal decrease in estrogen, aging, immobilization, vitamin D defi-

Table 5.1 Summary of bone remodeling disorders

Bone remodeling disorders	Common features
Osteoporosis	The most common disorder of bone remodeling. It is associated with low bone mass and disruption of the normal remodeling of bone leading to increased bone fragility and fracture. Several mechanisms can lead to the development of osteoporosis including postmenopausal decrease in estrogen; aging; immobilization; vitamin D deficiency; and medications
Chronic kidney disease-mineral and bone disorder	Refers to multiple defects in bone related to chronic kidney disease. Chief among them is the effect of kidney disease on the levels of parathyroid hormone (PTH). PTH can be low or high dependent upon the cause of chronic kidney disease. Elevated PTH can lead to increased remodeling and low PTH can lead to decreased remodeling. This disrupts the normal bone mineralization and leads to disorder of the bone matrix and weakened, diseased bone that is prone to fracture
Paget's disease of the bone	This represents localized areas of high bone remodeling (or turnover) and is the second most common disorder of bone remodeling. It is felt to represent a disorder of increased resorption followed by a secondary increase in bone formation. Its hallmark feature is increased bone remodeling that leads to bone overgrowth at sites of active disease
Osteopetrosis	This refers to multiple rare conditions that cause impaired osteoclast activity or development. It is characterized by increased bone density that is a result of diminished osteoclast activity which leads to decreased bone resorption. They are inherited disorders that can be autosomal recessive or dominant

ciency, and medications. An entire chapter is dedicated to osteoporosis and will not be discussed in depth in this chapter.

5.1.1.2 Chronic Kidney Disease-Mineral and Bone Disorder

Chronic kidney disease-mineral and bone disorder (CKD-MBD) refers to multiple defects in bone related to chronic kidney disease [2]. Renal osteodystrophy refers to the histology of bone disease that can only be proven with bone biopsy. This is a relatively new definition proposed in 2003 [3]. Previously, renal osteodystrophy referred to how bone remodeling is disrupted in a variety of ways in patients with chronic kidney disease.

Chief among patients with CKD-MBD is the effect of kidney disease on the levels of parathyroid hormone (PTH) [1, 4]. Depending on the cause of chronic kidney disease, PTH can be low or high. Elevated PTH can lead to increased remodeling and low PTH can lead to decreased remodeling. This change in the rate of remodeling disrupts the normal bone mineralization and leads to disorder of the bone matrix. This weakened, diseased bone is prone to fracture. As outlined in the osteomalacia chapter, chronic kidney disease is also associated with elevated fibroblast growth factor 23 and hypophosphatemia which can cause osteomalacia.

5.1.1.3 Paget's Disease of the Bone

Paget's disease of the bone, which is a separate disease from Paget's disease of the breast, will be elaborated on in greater detail later in this chapter. Paget's disease of the bone (which will be referred to as Paget's disease for the duration of the bone chapters) represents localized areas of high bone remodeling (or turnover) and is the second most common disorder of bone remodeling. Paget's disease is felt to represent a disorder of increased resorption followed by a secondary increase in bone formation. This results in the development of abnormal bone formation and disease manifestation.

5.1.1.4 Osteopetrosis

A final example of a bone remodeling disorder is osteopetrosis. Osteopetrosis refers to multiple rare conditions that cause impaired osteoclast activity or development. This is characterized by increased bone density that is a result of diminished osteoclast activity which leads to decreased bone resorption [5]. Osteopetrosis is an inherited disorder that can be autosomal recessive or dominant [6] and results from a variety of mutations that affect various aspects of osteoclast activity [1].

5.1.2 History

Bone remodeling disorders can present with a variety of symptoms. Some patients are symptom-free with incidental radiographic or laboratory findings. Others have bone pain or fractures which can result from minimal trauma. When disruption of normal bone remodeling is a concern, the patient's history should focus on several factors. Certain aspects of their lifestyle should be addressed: smoking history, physical activity level, nutritional status, personal history of fractures (both traumatic and nontraumatic), and family history of bone disease. History of falls should be assessed to determine risk for additional fractures. Finally, patients should be questioned about their safety as multiple fractures could be a sign of abuse.

5.1.3 Physical Exam

The physical exam should focus on a thorough musculoskeletal examination to evaluate for bone and joint tenderness and to identify any musculoskeletal deformities. A neurologic assessment is necessary to determine if the patient has any cranial nerve deficits or gait abnormalities. Cranial nerve impingement can be a result of excess bone formation and entrapment. Gait assessment is not to diagnose a bone remodeling disorder but

rather to help assess fall risk, which is important for treatment. Signs of multiple physical traumas (such as ecchymosis) and undernourishment should bring concern for abuse or neglect.

5.1.4 Diagnostic Workup

Workup for bone remodeling disorders begins with a clinical assessment. This includes the history and physical exam as well as a variety of other tests. There are certain laboratory findings and radiographic changes associated with the various causes of bone remodeling disorders. Basic labs can be obtained after clinical assessment which do not need to be fasting in most cases. Finally, a dual-energy X-ray absorptiometry (DXA) should be obtained for most patients with other images in certain situations. Specifics will be reviewed next.

5.1.4.1 Laboratory Abnormalities

Initial labs that should be checked in the evaluation of bone remodeling disorders are variable based on the diagnosis under consideration [1]. Labs to be checked in the evaluation of suspected Paget's disease will be discussed in further detail later on. To aid in the evaluation of osteoporosis, the following labs should be checked: electrolytes, phosphorus, creatinine, alkaline phosphatase, calcium, 25-vitamin D, and complete blood cell count. Additional labs for patients with low bone density and osteoporosis should be considered based on patient demographics and are discussed further in the osteoporosis chapter.

For CKD-MBD patients, PTH and 1,25-hydroxyvitamin D (calcitriol) should also be checked. There is some evidence that PTH and alkaline phosphatase may help in the differentiation of types of CKD-MBD, but it cannot be used definitively [7]. No laboratory findings can rule out osteoporosis in patients with CKD-MBD.

If osteopetrosis is a concern, review basic labs, such as those checked in the evaluation of osteoporosis. Although no labs are necessary to make the diagnosis of osteopetrosis, they can help rule out other conditions. Imaging is pathognomonic and is all that is required for diagnosis [5]. Genetic testing is also recommended to help predict specific complications of the varying genetic causes of osteopetrosis [5].

5.1.4.2 Radiographic Changes

A variety of radiographic changes can be seen depending on the etiology of the underlying bone remodeling disorder [1]. Imaging modalities and their associated changes in the setting of Paget's disease will be expanded upon later in this chapter. To establish a diagnosis of osteoporosis, the preferred imaging is DXA. Osteoporosis is defined as a T-score of −2.5 at any imaging site or a low-trauma fracture with low bone density on DXA [5]. This is discussed in detail in the osteoporosis section.

In CKD-MBD X-ray imaging may reveal osteopenia, demineralization of the cortical bone, subperiosteal resorption in the phalanges of the long fingers, sclerosis (thickening) of the vertebral bodies, potential soft tissue calcifications, and possible amyloid deposition [8]. There is no hallmark imaging in CKD-MBD that is diagnostic. Bone density by DXA does not distinguish between CKD-MBD and osteoporosis. Only bone biopsy can distinguish these two disease processes [9].

In the setting of osteopetrosis, X-ray imaging can reveal an Erlenmeyer flask deformity of the long bones. This refers to constriction of the diaphysis and flaring of the metaphysis, also known as metaphyseal flaring. Other findings include bone-within-bone appearance of imaged bone and end plate sclerosis with lucency of central vertebral bodies. These characteristic radiographic findings are diagnostic and are all that is needed to diagnose osteopetrosis.

5.1.4.3 Role of Bone Biopsy

Bone biopsies are not routinely performed in the diagnosis of osteoporosis, Paget's disease, or osteopetrosis but can be useful in CKD-MBD. Tetracycline-labeled transiliac bone biopsies are the gold standard for diagnosis of renal osteodystrophy. Bone biopsy can help differentiate the type of bone disease in CKD-MBD as

well as differentiate between one of these causes and osteoporosis [9, 10].

5.2 Treatment of Bone Remodeling Disorders

The treatments of osteoporosis and osteoporosis in chronic renal disease are addressed in the osteoporosis chapter in depth. Treatment of Paget's disease will be discussed later in this chapter. This section will focus on treatment of other bone remodeling disorders.

All patients at increased risk for fracture should be counseled on fall precaution. This may include having a physical therapist evaluate and treat for strength. Safety evaluations for home fall risks are important as well in all patients with increased fracture risk.

Treatment of CKD-MBD focuses on normalization of PTH [1, 3]. Phosphate binders can be used in the setting of elevated PTH. Calcimimetic agents can be used as well once any underlying concurrent vitamin D deficiencies have been normalized. In the setting of low PTH, treatment focuses on the reversal of this and typically requires reducing vitamin D and/or calcium levels if they are elevated through dietary changes [4]. No osteoporosis treatments have been well studied in CKD-MBD. Bisphosphonates and denosumab (antiresorptive agents) should be avoided in adynamic bone disease from CKD-MBD [9]. There may be a role for teriparatide (an anabolic agent) in adynamic bone disease, but it is unclear at this point in which kidney patients this should be used [11]. More can be found on these treatments in the osteoporosis chapter.

Treatment for osteopetrosis is supportive. Various therapies including vitamin D, interferon, steroids, and calcium restriction have not been successful. A multidisciplinary approach should be undertaken to treat fractures, nerve impingements, and vitamin D or calcium deficiency [5]. Surgery by an orthopedic surgeon is often necessary for fracture repairs. Neurosurgeons may need to decompress entrapped nerves.

5.3 Diagnosis of Paget's Disease of the Bone

Paget's disease can manifest itself as increased bone growth at single (monostotic) or multiple (polyostotic) sites throughout the body. More common areas of occurrence include the spine, lower extremity long bones, pelvis, and skull.

5.3.1 History and Clinical Presentation

The majority of patients with Paget's disease do not have any symptoms. If patients develop symptoms, the most common symptom is pain in the area of active disease. This typically manifests later on in the disease course and is often described as an achy pain. Bone deformities of involved areas are also common presenting symptoms. Depending on areas of disease involvement, other symptoms can manifest to various degrees. Spine and pelvic bone involvement can cause spinal cord compression. Long bone involvement can result in bowing of the bone and visible deformities. Involvement of the skull can impinge the cochlear-vestibular system and lead to hearing loss, dizziness, and vertigo among other symptoms. Paget's disease is associated with an increased risk of various bone tumors including osteosarcoma. Osteosarcoma tends to be minimally responsive to therapy. These tend to occur in the setting of long-standing, polyostotic disease [12]. Benign giant cell tumors can also occur (typically in the axial skeleton).

5.3.2 Physical Exam

The physical exam should focus on a thorough musculoskeletal examination to evaluate for bone and/or joint tenderness. Muscle and skeletal deformities should be looked for on exam as well as a neuro exam to look for signs of cord compression. This should include cranial nerve testing to focus on vision and hearing loss as Paget's disease can manifest as cranial nerve impingement.

5.3.3 Differential Diagnosis

Several other disorders should be considered when the diagnosis of Paget's is on the differential [13]. Osteomalacia (discussed in a separate chapter) can present with similar symptoms and laboratory findings, but radiographic changes of Paget's are not seen in osteomalacia. Metastatic disease can cause similar changes on imaging with both lytic and sclerotic lesions occurring. In Paget's disease, however, new lesions tend not to occur over time on bone scans. Seeing new lesions raises the concern for metastatic disease.

5.3.4 Diagnostic Workup

In addition to a thorough history and physical exam findings, there are certain laboratory findings and radiographic changes associated with Paget's disease. Alkaline phosphatase is elevated and is a hallmark of disease activity. Radiographs have diagnostic and standard appearances in Paget's disease of the bone. These abnormalities are outlined next.

5.3.4.1 Laboratory Abnormalities

Several labs should be included in the analysis of those with suspected Paget's disease. As with other bone remodeling disorders, the following labs should be checked: electrolytes, phosphorus, creatinine, calcium, and 25-vitamin D. Additional labs that should be included in the workup are those that can be affected by the rate in turnover [14]. Alkaline phosphatase tends to be elevated in Paget's disease, while serum calcium and phosphorus are normal. Serum C-telopeptide and urine N-telopeptide (both markers of bone resorption) are commonly elevated in the setting of active Paget's disease.

5.3.4.2 Radiographic Changes

Diagnosis of Paget's disease is aided by common changes seen in various diagnostic imaging modalities [8]. X-ray imaging can show differing changes depending on when in the disease process they are obtained. Earlier on, imaging typically shows osteolytic lesions in the skull among other areas. Later findings can show thickening and sclerosis of involved areas of the skeleton.

Nuclear bone scans are another modality used to evaluate Paget's disease and are more sensitive than X-ray imaging. Bone scans reveal increased uptake at sites of active disease. CT and/or MRI imaging can be considered for further evaluation of suspicious image findings if malignancy is of a concern.

5.3.4.3 Bone Biopsy

Biopsy is typically not required to make a diagnosis of Paget's disease. History, image, and lab findings make the diagnosis. If metastatic disease is in the differential, biopsy may be required in the presence of non-characteristic monostotic lesions. The majority of patients with Paget's disease do not undergo bone biopsy.

5.4 Pathogenesis of Paget's Disease of the Bone

Paget's disease is thought to represent a disease of osteoclast activity. Its hallmark feature is increased bone remodeling that leads to bone overgrowth at sites of active disease. There are a variety of genetic and environmental factors that contribute to the pathogenesis of Paget's disease. Osteoclasts from sites of active Paget's disease tend to be enlarged compared to normal areas of bone and have larger nucleolar bodies that are felt to play a role in disease development. The exact mechanism has yet to be elucidated.

5.5 Treatment of Paget's Disease of the Bone

Treatment of Paget's disease is aimed at easing symptoms and reducing bone turnover in certain situations [15]. Many cases require no therapy, and the patients are best served with clinical and laboratory monitoring only. The typical treatment for Paget's disease, if indicated, is bisphosphonate therapy. For severe complications of Paget's disease, surgery may be necessary.

5.5.1 Indications for Treatment

If patients have symptoms from their Paget's disease or are at risk for complications, they should undergo treatment. Symptomatic disease is characterized by bony pain at active sites and symptoms of nerve compression. Treatment should also be pursued in individuals who are symptom-free in the setting of certain criteria. In the setting of biochemically active disease at sites that can cause complications (skull, spine, areas adjacent to joints), treatment should be pursued as well. If serum alkaline phosphatase is greater than four times the upper limit of normal, treatment should be pursued in the setting of abnormal bone scans [16]. This is all in alignment with the Endocrine Society Guidelines which convey that all patients with biochemically active disease should be treated [13]. These are largely expert opinions; however, as there is only moderate evidence that treatments improve clinical outcomes, there is better evidence of decreased biochemical disease activity with treatment [17]. If there is hypercalcemia in an immobilized patient with polyostotic disease, treatment should be pursued as well [16]. Finally, if surgery is planned at the site of active Paget's disease, treatment should be given.

5.5.2 Treatment Options

Central to treatment is the use of bisphosphonate therapy [13, 16–18]. Choice of treatment is predicated on disease burden by some experts. In older patients or those with extreme disease burden, IV zoledronic acid is the preferred first-line treatment option. It is easier to administer, is more efficacious, and can last up to 2 years in terms of effectiveness for certain patients [19]. The Endocrine Society recommends intravenous zoledronic acid as the first-line therapy for Paget's disease [13]. Oral bisphosphonates such as alendronate and risedronate are preferred by some for treating younger patients or those with less extensive disease. For those that are intolerant of or have contraindications to bisphosphonates, calcitonin can be used as therapy [20]. This is preferred for older patients, patients who require a rapid improvement in their pain, and patients who are unable to take bisphosphonate therapy. Calcitonin is given subcutaneously for treatment of Paget's disease and tends to be used indefinitely as disease typically recurs when treatment is halted [20]. Prior to treatment, phosphorus, 25-vitamin D, and calcium should be normal. If they are not at goal, they should be addressed and repleted. Finally, denosumab may also be used for patients with renal dysfunction and Paget's disease, although there is limited data to support its use right now [21, 22].

5.5.3 Side Effects

Side effects of bisphosphonate therapy can present with a wide range of symptoms. The most common side effects of oral bisphosphonates are gastroesophageal reflux and other gastrointestinal symptoms. These complications can lead to poor patient adherence to oral bisphosphonate therapy. Patients can develop flu-like symptoms such as myalgias, fevers, and chills after IV bisphosphonate therapy. These symptoms are typically self-limited and may be avoided by administering Tylenol or calcium prior to IV treatments. A rare, potentially severe side effect of bisphosphonate therapy is osteonecrosis of the jaw. This complication is typically seen in patients receiving high-dose antiresorptive therapy and in patients with cancer. Patients with Paget's disease have been reported to have jaw osteonecrosis [23], but their connection to bisphosphonate therapy is not clear [17, 24]. The dose of IV bisphosphonates is much lower for patients with Paget's disease and osteoporosis, and osteonecrosis of the jaw is rarely seen after treatment for these conditions [25]. Calcitonin can cause nausea, vomiting, or flushing.

5.5.4 Monitoring

Alkaline phosphatase should be monitored every 3–6 months once therapy is initiated until it stabilizes when it can be measured yearly [26]. The Endocrine Society recommends monitoring based

on the choice of therapy. They recommend checking labs every 1–2 years after zoledronic acid infusion and every 6–12 months if oral bisphosphonates are used [13]. Normalized alkaline phosphatase should be used as a hallmark of disease remission. Imaging studies (CT or MRI) should be pursued if bone pain does not improve or respond to medical therapy. Bone scans are typically not used for monitoring of treatment response.

5.5.5 Retreatment

Consideration for retreatment focuses on evidence of disease recurrence. This is typically discovered by finding increased bone turnover markers on lab testing [13]. Alkaline phosphatase is the standard laboratory test to evaluate disease activity. Clinical indicators can be useful too. Increased pain can be a sign of recurrent disease that should lead to consideration of additional treatments. Medications used for retreatment are similar to primary treatment, and monitoring should be the same as after primary treatment.

5.5.6 Surgery

Surgical resection remains an option for treatment in the setting of deformities, development of bone tumors, or treatment of fractures among other things [13]. This is reserved for patients with severe clinical courses. The average patient with Paget's disease will not require surgical intervention.

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6

Principles of Diagnosis and Treatment of Osteomalacia

Roger Harty and Morgan S. Jones

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the diagnosis and treatment of osteomalacia
- *Objective*: On completion of this unit, the learner should be able to describe, list, or identify the following:

1. Clinical manifestations of osteomalacia
2. Different causes of osteomalacia
3. Laboratory findings associated with the different causes of osteomalacia
4. Radiographic findings typical of osteomalacia
5. Hallmarks of treatment of osteomalacia

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6.1 Definition of Osteomalacia

Osteomalacia is a descriptive term and diagnosis of diminished bone mineralization that can occur in both adults and children. Rickets, which only occurs in children, refers to a process at the growth plates. It cannot occur in adults as their growth plates have already closed. In children, osteomalacia is often accompanied by rickets.

Osteomalacia occurs at sites of bone turnover and is characterized by decreased bone mineralization. It is caused by hypocalcemia, hypophosphatemia, inhibition of bone mineralization, or a combination of these mechanisms. Several pathologic processes that disrupt calcium, phosphorus, or vitamin D regulation cause osteomalacia. The most common reason for osteomalacia is vitamin D deficiency. Patients frequently suffer from pain or fractures. Clinical presentation, causes, and treatment are explored further in this chapter.

6.1.1 Clinical Presentation

Osteomalacia can present with a variety of symptoms and clinical severity. Symptoms range from asymptomatic with radiographic abnormalities to bone pain and fractures. Low trauma fracturing can be a hallmark of the disorder [1].

The most common symptom is pain [2]. The bone pain is thought to be secondary to the hydrated matrix being pushed outward on the periosteum of the mineralized bone [3]. Patients typically complain of a dull ache that throbs. Bone pain is typically worse with activity and can become severe. This pain tends to be more common in the lower extremities, pelvis, or lumbar spine. Tenderness is a common characteristic of this pain as well. Rest rarely causes complete remission of the pain, and most patients report chronic and constant pain. Many patients are able to describe bone pain and distinguish it from other types of pain to clinicians with a careful history [4].

Patients with osteomalacia have an increased risk of fractures. Specifically there are higher rates of fracture seen in the long bones, the vertebral bodies, and the ribs [5]. The most common region for fractures is in the subtrochanteric region of the femur or metatarsals which bear the greatest load in the human body [4]. Muscle weakness can also occur but is less frequent. Proximal muscle weakness can be the initial presentation in some patients [6]. This often leads to atrophy of the muscles and can cause the development of gait abnormalities and proximal muscle weakness.

Osteomalacia is often related to hypocalcemia. Symptoms of hypocalcemia may be present in patients with osteomalacia. These symptoms include cramps, muscle spasms, and perioral numbness and tingling [4].

A full history should be obtained when a patient has a fracture or bone pain. In patients with osteomalacia, a full fracture history may reveal previous low trauma or frequent fractures. It is important to question about vitamin D and calcium intake as well as exposure to sunlight since this is key to vitamin D synthesis. When evaluating vitamin D and calcium intake, it is important to determine if the patient has any signs or symptoms consistent with malabsorption.

Patients must be questioned about symptoms of malabsorption including diarrhea. Malabsorption of vitamin D or calcium can result in osteomalacia. Inflammatory bowel diseases and celiac disease are common culprits. A growing number of people are undergoing gastric surgeries including bypass that can also lead to calcium or vitamin D deficiency after the procedure. As many as 65% of patients may have vitamin D deficiency, and an equally high number have elevated parathyroid hormone (PTH) after Roux-en-Y gastric bypass [7]. The elevated PTH is secondary to vitamin D and possibly calcium deficiency. These problems can lead to poor bone health and osteomalacia in severe cases.

Family history can be important for discovering rare genetic disorders. Patients that have experienced fractures must also be questioned about falls and traumas. This can help determine if a patient should undergo further workup for osteomalacia or other bone disorders.

6.1.2 Pathogenesis

As discussed in previously, the trabecular network of bones is constantly undergoing remodeling by osteoblast and osteoclast activity. Osteoblasts lead to the formation of osteoid (the organic matrix of bone) that then undergoes further changes that lead to calcification and mature bone formation. Osteomalacia disrupts this process which leads to demineralization and improper bone formation through the development of improper bone matrices. As reviewed earlier in this book, proper bone mineralization and development is predicated on a variety of factors. Disruption of the normal metabolism of calcium, phosphate, or alkaline phosphatase plays a role in osteomalacia. Acid-base balance and the disruption of pH can lead to defective mineralization of bone and osteomalacia.

Vitamin D deficiency is the most common cause of osteomalacia. Vitamin D is a key hormone for properly functioning bone as well as for proper calcium and phosphorus regulation. Vitamin D synthesis was reviewed earlier. A good understanding of this pathway helps to understand causes of vitamin D deficiency among various parts of the vitamin D synthesis pathway. A decrease in vitamin D levels or activity leads to decreased bone resorption. Hypocalcemia occurs due to decreased intestinal absorption and increased calcium secretion through the urine in this setting. When this happens, PTH elevates which increases bone resorption [8]. Finally, phosphorus is excreted in excess through the urine. There are four mechanisms for vitamin D deficiency or resistance in osteomalacia: inadequate dietary or environmental availability of vitamin D, decreased 25-hydroxylation of vitamin D in the liver, decreased 1-alpha-hydroxylation of vitamin D in the kidneys, and end-organ insensitivity to vitamin D (Table 6.1) [9]. The most common is inadequate dietary or environmental availability.

Many groups of patients are at risk for vitamin D deficiency. Elderly patients with poor nutritional intake and low exposure to sunlight are at risk. People with dark skin and low exposure to sunlight are at risk as well. Finally, immigrant populations have been found to be especially vulnerable [5]. Also at risk for vitamin D deficiency are patients with malabsorption from primary gastrointestinal disease or after gastric bypass surgery. Patients with renal or liver disease are at risk for osteomalacia due the inability to synthesize 1,25-hydroxyvitamin D properly (calcitriol).

Table 6.1 Causes of osteomalacia

Mechanism of vitamin D deficiency/resistance	Potential etiologies
Inadequate dietary/ environmental availability	Gastrointestinal malabsorption Diminished exposure to sunlight History of gastric surgery (bypass) Low dietary availability
Decreased 25-hydroxylation in the liver	Cirrhosis
Decreased 1-alpha-hydroxylation in the kidneys	Renal failure Hypoparathyroidism
End-organ insensitivity	Hereditary vitamin D-resistant rickets

6.1.3 Differential Diagnosis

The signs and symptoms of osteomalacia are nonspecific and can represent the manifestations of other disorders that need to be considered. The differential diagnosis for osteomalacia should include primary hyperparathyroidism, Paget's disease of the bone, osteoporosis, and malignancies, especially multiple myeloma. All these conditions may lead to low trauma fractures. Physical exam, history, laboratory findings, and radiographic changes help differentiate osteomalacia from these other bone disorders.

Osteoporosis (discussed in greater detail in another chapter) is associated with a similar clinical presentation, but physical exam and laboratory findings (normal calcium, phosphate, alkaline phosphatase) tend to separate this disorder from osteomalacia. Paget's disease (see the Paget's disease section in the bone remodeling disorder chapter for further details) typically differs from osteomalacia on a radiographic level. Typical radiographic changes with Paget's

disease include cortical thickening, coarse trabeculae, and areas of radiolucency and sclerosis which are not seen with osteomalacia. Primary hyperparathyroidism differs from osteomalacia with congruently elevated parathyroid hormone and elevated calcium levels. Multiple myeloma tends to differ radiographically with the presence of lytic lesions and associated laboratory findings of anemia, diminished renal function reflected by elevated creatinine, and hypercalcemia. A quick reference between these diagnoses is outlined in Table 6.2.

Table 6.2 Differential diagnosis of osteomalacia

Differential diagnosis	How disease manifestation differs from osteomalacia
Osteoporosis	Associated with a similar clinical presentation but physical exam and laboratory findings (normal calcium, phosphate, alkaline phosphatase) tend to separate this disorder from osteomalacia
Paget's disease of the bone	Typical radiographic changes with Paget's disease include cortical thickening, coarse trabeculae, and areas of radiolucency and sclerosis (which are not seen with osteomalacia)
Primary hyperparathyroidism	Differs from osteomalacia with congruently elevated parathyroid hormone and elevated calcium levels
Multiple myeloma	Differs radiographically with the presence of lytic lesions and associated laboratory findings of anemia; diminished renal function reflected by elevated creatinine and hypercalcemia

6.1.4 Common Etiologies of Osteomalacia

There are several ways in which osteomalacia can develop (Table 6.3). As described previously, vitamin D deficiency or resistance is the main cause of osteomalacia. Underlying renal disease can lead to the development of osteomalacia outside of decreased vitamin D synthesis. Hypophosphatemia, hypophosphatasia, and exposure to certain medications and minerals can all facilitate development of osteomalacia [10]. Several rare genetic disorders such as axial osteomalacia and fibrogenesis imperfecta have also been associated with developing osteomalacia. Rarely, osteomalacia may be the result of a paraneoplastic syndrome.

6.1.5 Physical Exam Findings

The physical exam should focus on a thorough musculoskeletal examination to evaluate for bone and joint tenderness. Muscle strength should be assessed symmetrically. Bone tenderness is an important clinical exam finding. In particular, tenderness is often seen in the tibial shins. It is useful to percuss over the ribs, pelvic girdle, or sternum in patients with mild to moderate disease [4].

Common physical exam findings of hypocalcemia can be seen in patients with osteomalacia and should be looked for during the physical exam. The classic physical exam findings seen with hypocalcemia are Trousseau's sign and Chvostek's sign. These signs are a result of neuromuscular irritability from latent tetany

Table 6.3 Lab findings in various types of osteomalacia

Cause of osteomalacia	Calcium	Phosphorus	25-Vitamin D	Alkaline phosphatase	FGF-23	PTH
Renal phosphate wasting	Normal	Low	Normal	Normal to elevated	Elevated	Normal
Renal tubule acidosis	Normal	Low	Normal	Normal	Elevated	Normal
Hypophosphatasia	Normal	Normal	Normal	Low	Normal	Normal
Tumor-induced osteomalacia	Normal	Low	Normal	Normal	Elevated	Normal
Vitamin D deficiency	Normal to low	Normal to low	Low	Elevated	Normal	Elevated
Fibrogenesis imperfecta	Normal	Normal	Normal	Normal to elevated	Normal	Normal

(intermittent muscular spasms) caused by low serum calcium levels [11]. Trousseau's sign is seen when a blood pressure cuff is inflated for an extended period (upward of 3 minutes). This leads to spasm of the carpal tendons causing flexion of the wrist, adduction of the thumb, extension of the interphalangeal joints, and flexion of the metacarpophalangeal joints. A positive Chvostek's sign is contraction of the facial muscles. Examiners trigger this sign by tapping on the facial nerve and then visualizing the contractions of the facial muscles.

6.1.6 Diagnostic Workup

A good diagnostic workup starts with the history and physical exam as stated previously. In addition, there are characteristic lab and radiographic findings for osteomalacia. Most of the laboratory evaluation can be obtained after the initial visit with the patient. There are no labs that require the patient to be fasting, and most are obtainable with a simple blood draw. In addition to blood draws, 24-hour urine collections are helpful in some patients.

6.1.6.1 Laboratory Abnormalities

Initial labs checked in the evaluation of osteomalacia should include calcium, alkaline phosphatase, parathyroid hormone, 25-vitamin D, 1,25-vitamin D, phosphate, serum electrolytes, BUN, and serum creatinine [1]. These labs can be variable dependent on the cause of osteomalacia (Table 6.3). Fibroblast growth factor 23 (FGF-23) influences vitamin D metabolism. Elevated serum FGF-23 causes phosphorus wasting through the urine and hypophosphatemia. Although it is not routinely measured, it can be helpful in determining the cause of osteomalacia. Calcium excretion through the urine can also be helpful to determine if patients have inadequate dietary calcium intake.

For patients with osteomalacia related to nutritional deficits, typical lab findings reveal a low 25-hydroxyvitamin D (calcidiol). Normally the calcidiol concentration is less than 10 ng/dL [2, 4]. Patients also have low to low normal serum calcium and phosphate. Parathyroid hormone and alkaline phosphatase are typically elevated. If the patient has a dietary calcium deficiency, the 24-hour urine calcium collection will be low. Fibroblast growth factor 23 is typically normal [2].

When the underlying cause of osteomalacia is renal phosphate wasting, the lab profile is different. Serum phosphate is typically low. Calcium and calcidiol are normal. Parathyroid hormone and alkaline phosphatase tend to be normal to slightly elevated. Finally, calcitriol is typically elevated or inappropriately normal, while FGF-23 is often elevated.

For those with renal tubular acidosis, phosphate is low. Calcium, alkaline phosphatase, PTH, calcidiol, and calcitriol are all normal in this condition. Fibroblast growth factor 23 can be elevated [12]. In patients with hypophosphatasia, the alkaline phosphatase is the only typical abnormal lab finding. Alkaline phosphatase is low, while everything else is typically in the normal range. In tumor-induced osteomalacia (TIO), which is a rare paraneoplastic syndrome, elevated FGF-23 and hypophosphatemia are the hallmark. There are typically no lab abnormalities for fibrogenesis imperfecta, although alkaline phosphatase can be high [13]. Phosphorus, calcium, and the various vitamin D levels are typically normal.

6.1.6.2 Radiologic Changes

Various radiographic changes can be seen in osteomalacia. Typically the most common finding on X-ray imaging is cortical thinning of the bone [14]. More specific findings seen on X-ray include looser zones and vertebral body changes. Looser zones refer to characteristic narrow radiolucent lines (less than 5 mm in width with sclerotic bands) found on X-rays of individuals with osteomalacia [5]. They can typically be seen in the femoral neck or shaft but can also be found in the ribs, ulna, clavicle, or metatarsal bones. Decreased mineralization of the vertebra can lead to increased radiolucency of the vertebral bodies

on X-ray. Worsening of disease can lead to concave changes of the vertebral bodies.

6.1.6.3 Bone Mineral Density Changes

Dual-energy X-ray absorptiometry (DXA) is used to evaluate bone mineral density (BMD). The BMD can be normal, reduced, or increased depending on the etiology of osteomalacia. Patients with vitamin D deficiency or vitamin D-resistant osteomalacia often have low bone density that is in the osteopenia or osteoporosis range. This has been shown over a variety of ethnicities in men and women [1, 2, 15–17]. Other causes do not typically reveal low bone density and can even be higher than normal [18]. Typically DXA is not required to establish the diagnosis of osteomalacia as it is not specific and cannot distinguish osteomalacia from osteoporosis.

6.1.6.4 Bone Biopsy

The most accurate means of diagnosing osteomalacia is through bone biopsy with tetracycline labeling. Typically biopsy results reveal increased osteoid volume, widening of osteoid seams, and prolonged lag time of mineralization [19]. Bone biopsy is not frequently pursued because of its invasive nature and based on the fact that diagnosis can be readily made from clinical and laboratory findings. In addition, for bone biopsy to be pursued, it should be done at a medical center familiar with interpreting tetracycline-labeled bone biopsies.

6.2 Etiology of Osteomalacia

The manifestations of osteomalacia can result from a variety of disorders that lead to findings pathognomonic for osteomalacia. Specific causes or osteomalacia will be reviewed in greater depth next.

6.2.1 Vitamin D Deficiency

The most common cause of osteomalacia is vitamin D deficiency [3]. Vitamin D plays a variety of roles in the body. These include, but are not limited to, the stimulation of intestinal calcium and phosphate absorption and increased reabsorption of calcium in the distal tubules of the kidneys. Hypocalcemia and hypophosphatemia can therefore be the result of vitamin D deficiency or resistance. Malnutrition can lead to decreased vitamin D levels regardless of the presence or absence of malabsorptive disorders. Underlying liver disease and renal disease can disrupt the normal processing of vitamin D diminishing its activation and proper functioning. Certain genetic disorders lead to vitamin D resistance.

6.2.2 Renal Disease

Underlying renal disorders can also lead to the development of osteomalacia. Chronic kidney disease resultant from a variety of causes can lead to decreased conversion of calcidiol to calcitriol and lead to the development of osteomalacia [3]. Proximal renal tubule acidosis (type 2 RTA) causes proximal phosphate wasting in the renal tubules. This subsequently results in metabolic acidosis, and, as a compensatory mechanism, there is increased calcium loss which contributes to the development of osteomalacia [20].

6.2.3 Medications

Exposure to several medications and excess exposure to certain minerals can also cause osteomalacia. Exposure to certain bisphosphonates, a hallmark of treatment for osteoporosis, can inhibit bone mineralization and lead to the development of osteomalacia. Specifically, nonnitrogenous bisphosphonates are associated with osteomalacia. Etidronate has been linked to osteomalacia [21, 22]. However, there is conflicting evidence for this across different patient populations. It is clear that patients with Paget's disease of the bone may develop osteomalacia [21, 22], but it is unclear if it happens in patients with osteoporosis. Some studies have suggested etidronate is safe for osteoporosis [23]. Regardless, the currently used bisphosphonates in the United States (alendronate, ibandronate,

risedronate, and zoledronic acid) are all nitrogen containing and are not associated with osteomalacia.

Other medications that are used in a variety of clinical settings can cause osteomalacia. Some medications used to treat human immunodeficiency virus (HIV) have been associated with osteomalacia. This is due to medication-induced hypophosphatemia. Specifically, the antivirals tenofovir and adefovir have been implicated [24, 25]. Valproic acid increases catabolism of calcitriol leading to calcitriol deficiency and osteomalacia [26]. Intravenous ferric carboxymaltose, which is used for iron deficiency anemia, can also induce osteomalacia [27].

Excess aluminum exposure, typically seen in those on total parenteral nutrition, can also inhibit bone mineralization [28]. Similarly, exposure to excess amounts of fluoride, found in toothpaste and certain teas, can also lead to the development of osteomalacia [29]. This is a rare cause of osteomalacia that requires high exposure quantities of tea or toothpaste to impact the bone. Typical toothpaste use or tea consumption does not negatively impact bone health.

6.2.4 Hypophosphatemia

Hypophosphatemia as a result of vitamin D deficiency or renal phosphate wasting can also lead to the development of osteomalacia. Primary renal phosphate wasting syndrome can be either acquired or inherited. Fibroblast growth factor 23 excess is implicated in the pathogenesis. Several medications can lead to renal phosphate wasting as mentioned above too. Common medications causing this include valproic acid, cadmium, HIV medications, ferric carboxymaltose, and aminoglycoside antibiotics to name but a few [30].

6.2.5 Hypophosphatasia

Hypophosphatasia is a rare inherited disorder that can manifest itself in a variety of manners including the development of osteomalacia. This disorder involves various mutations in the tissue-nonspecific alkaline phosphatase (TNSALP) gene [31]. This leads to accumulation of various TNSALP substrates including an inhibitor of bone mineralization, pyrophosphate. Ultimately, the increase in TNSALP substrates can lead to the development of osteomalacia.

6.2.6 Tumor-Induced Osteomalacia

Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome. It is also known as oncogenic osteomalacia. The syndrome is mediated by FGF-23 which, as mentioned earlier, causes phosphate wasting [32]. Tumors that cause this rare disorder are typically benign but may be malignant. As of 2011, 337 cases of primary TIO had been reported with 200 cases being reported between 2001 and 2011 [33]. This suggests that the condition is being recognized more often. Patients typically present with bone pain and fractures.

6.2.7 Rare Causes

Finally there are two rare inherited disorders that can cause the development of osteomalacia: axial osteomalacia and fibrogenesis imperfecta. Axial osteomalacia is thought to result from an osteoblast defect (pathogenesis is uncertain) and is typically associated with osteomalacia of the axial skeleton (most often the cervical spine) [34]. The etiology of fibrogenesis imperfecta is unclear but results in the absence of collagen fibrils in the bone matrix as well as results in osteomalacia [35].

6.3 Treatment

Treatment of osteomalacia focuses on correction of underlying nutrient deficiency and reversal of the underlying disorder. Vitamin D and calcium supplements are the mainstay of therapy. For those with RTA in addition to vitamin D replacement, acidosis can be corrected with sodium citrate or potassium citrate. Hypophosphatemia has few established treatments, and there are no

established therapies for axial osteomalacia and fibrogenesis imperfecta, although some have been explored [13]. Tumor-induced osteomalacia treatment is resection of the tumor causing the paraneoplastic syndrome.

Vitamin D replacement is done with oral supplements or with light treatments. The recommended daily intake is 800 international units. In the setting of more severe vitamin D deficiency, the recommended replacement is 50,000 international units (IU) of vitamin D weekly for 8 weeks using ergocalciferol (vitamin D2) or cholecalciferol (vitamin D3). This is followed by 1000 IU of vitamin D daily typically using cholecalciferol. For those with underlying malabsorption, daily doses of 10,000 IU of Vitamin D may be needed [36]. In the setting of underlying liver or kidney disease, standard vitamin D replacement using cholecalciferol or ergocalciferol will not be effective, and calcitriol may be needed for replacement. .

Correction of underlying vitamin D deficiency can quickly lead to minimization of bone tenderness and improved muscle strength in a matter of weeks [15]. Within months, bone mineral density can improve. Serum calcium should be monitored to avoid overtreatment and the development of hypercalcemia. Calcidiol levels should be monitored routinely. Goal calcidiol levels are controversial. The Institute of Medicine recommends maintaining a 25-hydroxyvitamin D level between 20 ng/dL and 40 ng/dL [37]. Other professional societies, including the Endocrine Society, recommend a 25-hydroxyvitamin D level between 30 ng/dL and 50 ng/dL [38]. Depending on the etiology/length of time that osteomalacia has been present, osteomalacia can take months to years to resolve.

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Principles of Diagnosis and Treatment of Osteoporosis

7

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Contents

Goals and Objectives

- *Goal*: To introduce the reader to osteoporosis and explore various treatment strategies
- *Objective*: On completion of this unit, the learner should be able to describe, list, or identify:
  1. The definition of osteoporosis, osteopenia, and low bone density
  2. Factors that contribute to osteoporosis
  3. Ways to diagnose low bone density and osteoporosis

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4. Clinical consequences of osteoporosis including common fractures in osteoporosis
5. Treatments available for osteoporosis

7.1 Introduction

Osteoporosis is a skeletal disorder defined by propensity for low trauma fractures (fragility fractures) and low bone mineral density (BMD). This chronic medical condition can lead to significant morbidity and mortality; and its impact is especially felt in aging populations. Advancing age is a risk factor for osteoporosis. Sex is also a risk factor as women are more affected than men. According to the Centers for Disease Control and Prevention, 24.5% of women over the age of 65 and 5.1% of men over the age of 65 in the United States (USA) had osteoporosis between 2005 and 2010 [1]. All races and ethnicities are affected although there is higher prevalence in Caucasians [1]. Over 10% of community-dwelling adults are estimated to have osteoporosis in the USA [2]. Osteoporosis majorly contributes to the 4698 fractures per 100,000 person-years in women aged 50 and over although some high-impact fractures are not attributable to osteoporosis [2]. Fractures lead to an estimated 430,000 hospitalizations and $17 billion annually [2]. This is not just a problem in the USA. A study of European Union (EU) countries revealed that 22 million women and 5.5 million men were estimated to have osteoporosis across 27 EU countries in 2010 with an economic burden over 30 billion US dollars (37 billion euros) [3]. There are also multiple studies across Asia, Africa, Latin America, and the rest of the world revealing high incidence and cost to society [4]. In 2010 it was estimated that 21 million men and 137 million women over age 50 have a high fracture risk [5]. Truly, osteoporosis is a global health concern.

7.2 Important Definitions

Prior to discussing the clinical features and pathophysiology of osteoporosis, it is important to review clinical definitions. The diagnosis of osteoporosis is based on bone density measurements using dual-energy X-ray absorptiometry (DXA) in conjunction with fracture history. The World Health Organization (WHO) uses a young adult reference range to define the diagnosis of osteoporosis. The WHO defines a T-score of −2.5 standard deviations or below as diagnostic of osteoporosis [6, 7]. From this definition comes the basis for many of the terms used throughout this chapter. The T-score and Z-score are important values when interpreting a DXA and will be defined below (Table 7.1) along with many other important terms.

Bone Mineral Density (BMD) A measure of bone mineral architecture and strength that has been correlated with fracture risk.

Low Trauma Fracture (Fragility Fracture) There is not a single definition for low trauma fractures. The general definition is a fracture in a person from low or no trauma that would not lead to a fracture in a patient with healthy bones. They typically affect the hips, spine, and wrist. Examples include femoral neck or wrist fractures after a fall from a standing height or compression fractures of the spine with no known trauma. Low trauma fracture, fragility frac-

Table 7.1 Classification of bone mineral disorders

	Bone mineral density by dual-energy X-ray absorptiometry
Low bone mineral density for age	Z-score ≤ -2.0[a]
Osteopenia[b]	T-score −1 to −2.5
Osteoporosis[b]	T-score ≤ -2.5 or T-score −1 to −2.5 with history of fragility fracture
Severe osteoporosis[b]	T-score ≤ -3.5 or T-score ≤ -2.5 with history of fragility fracture

[a]Z-scores are based on age-matched controls
[b]Definitions apply to postmenopausal women and men aged ≥50

ture, and major osteoporotic fracture are used interchangeably in this chapter.

Dual-Energy X-ray Absorptiometry (DXA) An imaging modality using X-ray to calculate bone mineral density. Typically, the BMD of the lumbar spine, total femur, and femoral neck is measured. The forearm and other areas are calculated in special clinical situations.

T-score This is a standardized measurement to compare a patient's BMD to a young healthy reference range. The WHO recommends using the National Health and Nutrition Survey III database [6, 7]. By this standard, the T-score compares BMD to young, healthy Caucasian women. This is used in postmenopausal women of any age and men over 50 years of age.

Z-score A standardized measurement to compare a patient's BMD to an age-, race-, ethnicity-, and sex-matched population. This is used in premenopausal women of any age and men less than 50 years of age.

Normal Bone Density In regard to a DXA, this relates to a T-score of ≥ -1 for a postmenopausal woman or a man over the age of 50. However, there is no clearly defined upper limit of normal. In premenopausal women or men less than 50 years of age, normal bone density is more debatable as there is less clinical evidence to support a normal range. In general a Z-score ≥ -2 is considered normal.

Osteopenia This is a low bone density condition. It is defined as a T-score > -2.5 and ≤ -1. Osteopenia is not applied to young men less than 50 years old or premenopausal women in general.

Lower Than Expected Bone Density for Age This refers to a Z-score of ≤ -2. It is often used instead of the term osteoporosis for premenopausal women and men less than 50 years of age.

Osteoporosis This is a low bone density condition. It is defined as a T-score of ≤ -2.5 or a bone density in the osteopenia range with a low trauma fracture.

Severe Osteoporosis This is defined as a bone density with a T-score of ≤ -3.5 or ≤ -2.5 with a low trauma fracture.

Low Bone Density This may refer to osteopenia, osteoporosis, or lower than expected bone density for age.

7.3 Pathophysiology of Osteoporosis

In children and adolescents, osteoblasts predominate in forming new cortical bone allowing enlargement of the skeleton. This initial formation is called modeling and involves endochondral bone formation in the development of long bones and vertebrae. After peak growth, the adult bone is constantly undergoing remodeling. The balance between bone resorption by osteoclasts and new bone formation by osteoblasts is directed by osteocytes [8] and must be maintained to prevent loss of bone strength and bone mass. This balance is under the influence of mineral, hormonal, and mechanical forces [9]. The different components of the bone remodeling unit are called the basic multicellular unit (BMU) and consist of osteoblasts, osteocytes, osteoclasts, and bone lining cells [10]. The BMU is impacted by multiple forces to either enhance or prevent proper bone remodeling. More on normal bone remodeling is in the chapter on basic bone metabolism.

In osteoporosis, there is either an oversupply of osteoclasts, causing bone resorption, or a deficiency of osteoblasts, leading to insufficient bone formation [9]. In addition, aging causes change to the function, size, and number of osteocytes [11, 12]. This complex interplay leads to changes in the bone microarchitecture leading to a fragile skeleton. The most prevalent cause of these

changes is related to sex hormone deficiency. Estrogen deficiency predisposes, but does not guarantee, osteoporosis.

7.3.1 Sex Hormone Deficiencies

Postmenopausal women are the most impacted demographic by osteoporosis. This is because of the certainty of estrogen deficiency after menopause and estrogen's effect on bone health. Normal menopause occurs after the age of 40. The average age of onset is in the early 50s. Effects of estrogen deficiency on bone health have been demonstrated in clinical research showing that women with an earlier age of menopause have a higher fracture risk and lower bone density [13].

Estrogen deficiency causes a variety of negative effects on bone health. These include increases in osteoblastogenesis, osteoclastogenesis, and the lifespan of osteoclasts, while there is a decrease in lifespan of osteoblasts and osteocytes [9, 14]. This leads to increased bone resorption relative to bone formation. A variety of molecular pathways and specific cytokines have been implicated. Interleukin-6 (IL-6) causes increased osteoclast formation and increased bone resorption [15]. Estrogen and androgen suppress IL-6, which likely helps prevent osteoporosis from developing.

Women may also develop estrogen deficiency prior to menopause. This typically happens after hysterectomy with bilateral oophorectomy. There are multiple indications for this surgery [16] and women who do not receive estrogen therapy after they are at risk for low bone density [17–19]. Bone density does not decline as quickly if estrogen is supplemented after surgery [17]. Other causes of estrogen deficiency in young women include primary ovarian insufficiency and hypogonadotropic hypogonadism. Functional amenorrhea is a form of hypogonadotropic hypogonadism that affects young women with low body weight due to excess exercising and weight loss. It can be seen in patients with anorexia and causes low bone density [20].

Men with testosterone (an androgen) deficiency are also at increased risk for osteoporosis. Clinical testosterone deficiency is called hypogonadism and is caused by testicular damage in primary hypogonadism. Secondary hypogonadism is caused by pituitary or hypothalamic dysfunction. Hypogonadal men have been shown to have lower bone density [21, 22]. Testosterone deficiency is also associated with faster decline in bone density in aging males [21]. Replacing testosterone in hypogonadal men has been shown to increase bone density, but fracture reduction has not been demonstrated [22–25]. Testosterone is not the only sex hormone that plays an important role in the pathogenesis of osteoporosis in men. Estrogen plays an important role as well. In fact, estrogen is a better predictor of low bone density in aging males than testosterone level [21].

Although the exact effects of sex hormones are not yet well understood in the pathogenesis of osteoporosis, estrogen and testosterone play an important role. Hormone levels decline naturally with aging, but can also be caused by other pathologies or surgical procedures. Assessment of hormone status is important in diagnosis and treatment of patients with low bone density and osteoporosis.

7.3.2 Glucocorticoids and Other Medications

Multiple medications can affect bone density and fracture risk. Primary among them are systemic glucocorticoids. Other examples include antiepileptics (anticonvulsants), immunosuppressants, aromatase inhibitors, heparin, and some chemotherapies. Some medications have such a high correlation with low bone density and osteoporosis that preventative therapy is used. These include glucocorticoids and aromatase inhibitors.

Glucocorticoids are used as a potent anti-inflammatory for a variety of conditions. Many autoimmune disorders respond to long-term glucocorticoid therapies. Unfortunately, they have severe effects on the skeletal system. Decreased bone density and fractures can be seen in patients on doses of prednisone or prednisone equivalents greater than 2.5 mg per day and can occur only after a few months of therapy [26]. As many as 50% of patients on long-term glucocorticoid therapy develop fractures [27]. This is caused through multiple mechanisms.

Increased bone resorption with decreased bone formation is the mechanism by which glucocorticoids cause osteoporosis. Glucocorticoids act through receptor activator of nuclear factor kappa-B (RANK) and RANK ligand (RANKL). The RANK and RANKL stimulate osteoclastogenesis and osteoclast differentiation [28]. In addition, glucocorticoids decrease androgen in men and estrogen in women [29, 30], which causes the pathology outlined above. Calcium absorption in the gut and excretion through the urine are also affected by glucocorticoids. The action of glucocorticoids opposes vitamin D, and, with the net loss of calcium through the urine compared to absorption from the gut, parathyroid hormone (PTH) is increased [31–33]. This all leads to increased bone resorption. Finally, glucocorticoid suppresses bone formation by antagonizing the actions of PTH while decreasing synthesis of insulin-like growth factor and testosterone [34–36]. They also cause apoptosis in osteoblasts [34]. These combined effects have a net effect of decreased bone formation with increased resorption.

Aromatase inhibitors are frequently used to treat breast cancer. Although they can be valuable for treating breast cancer, they also lead to decreased peripheral estrogen and bone density loss [37]. The mechanism for declining bone health is the same as estrogen deficiency. However, compared to typical estrogen deficiency after menopause, aromatase inhibitors cause 2–4 times the bone loss [37]. A fracture risk of 18–20% is seen with aromatase inhibitor therapy [37]. Patients started on these therapies need close monitoring and are often given prophylactic treatments with bisphosphonates.

Anticonvulsants are also associated with decreased bone density and increased fracture risk. There appears to be a class effect, although the specifics are not well understood. Older anticonvulsants, including phenytoin, phenobarbital, carbamazepine, and valproate, are most associated with decreased BMD and fracture risk. Some anticonvulsants appear to increase the metabolism of 1,25-hydroxyvitamin D (calcitriol) to 25-hydroxyvitamin D (calcidiol) by inducing hepatic enzymes. This has been shown with some, but not all, anticonvulsants that are associated with increased fracture risk [38]. Regardless of the mechanism, anticonvulsants carry a 1.2- to 2.4-fold increased risk of fracture [38]. Patients with epilepsy on anticonvulsants should be screened for osteoporosis.

7.3.3 Other Factors

There are a variety of other factors that influence bone density. These factors include vitamin D, PTH, and thyroid hormones. Excesses or deficiencies of these substances influence bone density and can lead to osteoporosis. Primary hyperparathyroidism, hyperthyroidism, vitamin D deficiency, and a variety of other conditions all are associated with low BMD and osteoporosis (Table 7.2).

Table 7.2 Secondary causes of osteoporosis and low bone density

Diseases	Hyperparathyroidism Hyperthyroidism Hypogonadism Hyperprolactinemia Hypercortisolism (Cushing's syndrome) Diabetes mellitus type I Rheumatoid arthritis Chronic obstructive pulmonary disease Chronic kidney disease Primary biliary cirrhosis/chronic hepatitis Inflammatory bowel disease Celiac disease Pancreatic insufficiency Anorexia nervosa Bone marrow dysfunction
Medications	Glucocorticoids Antiepileptics Aromatase inhibitors Cytotoxic medications (chemotherapy/ immunosuppression)
Congenital	Hypophosphatasia Osteogenesis imperfecta
Other	Immobility Gastric bypass/gastrectomy Malnutrition/alcoholism Solid organ/bone marrow transplant

Parathyroid hormone regulates calcium, phosphorus, and vitamin D in the body. It causes extraction of calcium and phosphorus from the bone through increasing the number of osteoclasts. Primary hyperparathyroidism is often an asymptomatic disease that presents with incidental hypercalcemia. Excess PTH exposure over long periods of time causes increased bone turnover and decreases BMD. This can lead to osteoporosis and fragility fractures. As many as 48% of patients with asymptomatic primary hyperparathyroidism have osteoporosis. The rates are higher in patients with primary hyperparathyroidism and known nephrolithiasis or bone disease [39]. The prevalence of osteoporosis in patients with primary hyperparathyroidism is higher than that of postmenopausal women [39]. Parathyroidectomy is often curative in primary hyperparathyroidism, and therefore this diagnosis should not be missed. Patients with osteoporosis and hypercalcemia should be tested for primary hyperparathyroidism.

Thyroid hormone, particularly liothyronine (T3), plays an important role in normal bone metabolism. Multiple interleukins are stimulated by T3, including IL-6, which leads to normal synthesis of bone matrix, and regulates proliferation and apoptosis of osteoblasts [40]. Hyperthyroidism leads to a hypermetabolic state and increased bone resorption. There are elevated levels of IL-6 in hyperthyroid patients. This leads to decreased bone density in 10–20% of patients with overt hyperthyroidism [40]. There is an increased risk of osteoporosis and fragility fractures in patients with hyperthyroidism as well [40]. Hip fracture risk is 2.5 times higher in patients with hyperthyroidism than those with normal thyroid function [41].

Severe vitamin D deficiency leads to osteomalacia. Typically the vitamin D levels are less than 10 ng/dL in osteomalacia [42, 43]. Milder vitamin D deficiency however can increase PTH and lead to increased bone turnover. This can cause osteoporosis or low BMD. Indeed, vitamin D deficiency is prevalent in as many as 71% of postmenopausal women and in approximately 50% of patients with osteoporosis [44]. Treatment is easy and well tolerated for vitamin D deficiency. All patients with osteoporosis should be screened for low vitamin D.

In addition, several other rare and common disorders affect bone density. Excess cortisol seen in patients with Cushing's syndrome or Cushing's disease is one such rare disease. Type 1 diabetes is an example of a more common condition that affects the bone. Table 7.2 lists these conditions as well as other factors that affect bone density.

7.4 Diagnosis of Osteoporosis

Diagnosing osteoporosis is generally straightforward. Patients with low trauma fractures should be evaluated for osteoporosis and so should patients at risk for developing osteoporosis. Evaluation of the patient begins with a thorough history and physical exam. Basic lab testing is important to rule out other causes of poor bone health and secondary causes of osteoporosis. Imaging with DXA is routinely performed in all patients with osteoporosis with other imaging in certain situations.

There is not a broad differential for patients with osteoporosis and a low trauma fracture. Osteomalacia is the primary consideration to be ruled out. Paget's disease of the bone, chronic kidney disease-metabolic bone disorder, multiple myeloma, metastatic cancer to the skeleton, and osteopetrosis are also on the differential. These conditions are easily differentiated with imaging and laboratory studies. Most of these conditions are discussed in depth elsewhere in this book.

The differential for the cause of osteoporosis is broad, however. There are several risk factors for developing secondary osteoporosis. Parathyroid disease, chronic kidney disease, vitamin D deficiency, liver disease, and thyroid disease all must be considered depending on the patient. Rather than ruling out all these conditions with routine lab testing, a clinician must evaluate the patient and select the appropriate tests based on the patient's history and presentation.

7.4.1 History

History for patients with osteoporosis, osteopenia, low trauma fracture, and low bone density for age must be comprehensive. A complete medical history including fracture history is imperative. When a fracture is discovered during history taking, it is important to determine the cause of the fracture. Did the patient fall from a standing height or were they in a motor vehicle collision? In addition, the location of the fracture is key. All patients should be questioned if they have had forearm fractures, hip fractures, or spinal compression fractures. These are the most common fractures in osteoporosis. Beyond personal fracture history, a family history is necessary as well. Family history of osteoporosis and hip fracture places a patient at risk for fracturing themselves.

A complete medication history is very important in patients with osteoporosis. As mentioned earlier, there are multiple medications associated with low bone density, osteoporosis, and fracture risk. The length of time the patient took the medication and dose should be clarified. Alcohol and smoking history also impacts bone health.

A good clinician will also inquire about symptoms related to secondary causes of osteoporosis. Hyperthyroidism should be suspected in patients with palpitations, unexpected weight loss, heat intolerance, diarrhea, and tremor. To evaluate for potential hyperparathyroidism, patients should be asked about nephrolithiasis and hematuria. A nutritional history should include vitamin D and calcium intake. Sunlight exposure history is also important to evaluate vitamin D status. Malabsorption disorders, including celiac disease, can impact bone health through vitamin D and calcium deficiency. Also inquire about gastrointestinal symptoms and symptoms of other vitamin deficiencies to determine further workup.

To further quantify fracture risk, the Fracture Risk Assessment Tool (FRAX) is useful. The FRAX score has been validated for postmenopausal women and men over 50 over a variety of races and ethnicities [45]. It is particularly useful tool in patients with osteopenia to determine treatment. Clinicians can find this tool online. It calculates fracture risk based on personal and family history of fracture, age, height, weight, sex, smoking and alcohol history, glucocorticoid use, rheumatoid arthritis history, secondary osteoporosis history, and femoral neck BMD [45]. Currently, it is available online for free at https://www.sheffield.ac.uk/FRAX.

Finally, it is important to assess for falls in patients with osteoporosis or other bone disorders. A fall history is important to identify risk factors and reduce future falls. A home assessment to reduce risk of fall at home may also be necessary. Clinicians should ask patients to identify any areas of concern in their house. These include cluttered hallways, steps, hallways without railings, and other fall hazards. Frequent unexplained falls with bruising and multiple fractures can be a sign of abuse or neglect. Patients must be evaluated for safety as well.

7.4.2 Physical Exam

The physical exam is similar to that for other bone disorders. A musculoskeletal exam is needed with a focus on palpation of the spine and hips to look for tenderness. It should include a patient's height as height loss can be a sign of osteoporosis or compression fractures in the vertebrae. Inspection of the teeth is important prior to bisphosphonate therapy. Patients with poor dentition may need dental clearance by their dentist prior to receiving bisphosphonate therapy. After the musculoskeletal exam, neurologic exam should be performed to assess gait and fall risk. This may include a physical therapist evaluation of the patient. The general physical exam and inspection of the patient should look for signs of abuse or neglect. Ecchymosis or signs of dehydration and malnutrition are warnings of this.

7.4.3 Diagnostic Workup

After the history and physical exam, laboratory testing followed by imaging is needed for most patients with suspected osteoporosis. Laboratory testing is focused on finding secondary causes and can generally be collected after the initial visit. Typically, these are blood tests that can be run at any time of the day and do not require the patient to be fasting. Exceptions are described below. This is followed by imaging which is normally diagnostic of osteoporosis.

7.4.3.1 Laboratory

Laboratory testing should be tailored to the individual patient. Lab tests for all patients with osteoporosis should include serum calcium, phosphorus, 25-hydroxyvitamin D, complete blood count, liver function tests, alkaline phosphatase, and creatinine level. These tests have no restriction on time of the day to run and do not require the patient to be fasting. As osteoporosis is less common in men, lab tests should also include a total testosterone and a 24-hour calcium secretion for male patients [25]. Testosterone should be measured between 8 AM and 10 AM and must be repeated to diagnose hypogonadism at least one additional time. If hypogonadism is diagnosed, it should be treated separately and concurrently with osteoporosis in men. Calcium secretion through the urine, as assessed by a 24-hour urine calcium, helps to determine nutritional calcium status. If low, a 24-hour urine calcium is suggestive of calcium deficiency. This test can also be run in women with suspected calcium deficiency in the setting of suspected or known malabsorption disorders or other dietary deficiencies.

Additional testing is based on clinical presentation. Patients with concerns for multiple myeloma should have a serum or urine electrophoresis. Concerning signs include anemia, elevated creatinine, and hypercalcemia. Patients with hypercalcemia or nephrolithiasis should also have a PTH collected. Finally, if there is concern for hyperthyroidism, a thyroid-stimulating hormone level should be collected.

7.4.3.2 Imaging

Patients with known osteoporosis should all have a DXA scan. The scan is diagnostic of osteoporosis as mentioned above in the definitions section. A DXA can also help rule out osteoporosis compared to other bone disorders. It is an important screening tool for patients at risk for osteoporosis and is used for monitoring therapy.

Women should be screened for osteoporosis at age 65 since being postmenopausal puts women at significant risk for osteoporosis [46]. Men and premenopausal women should not be screened, but the diagnosis should be considered in patients if clinically indicated. Men and premenopausal women with low trauma fractures should have a DXA scan. All patients with long-term glucocorticoid therapy should be clinically evaluated for bone health as well. A DXA should be obtained in these patients depending on their fracture risk [47]. Specifics are reviewed later in this chapter. Patients with long-term anticonvulsant therapy should also be screened with DXA, although this is not as well defined. Some suggest that screening take place after 3–5 years of therapy initiation [48].

Plain film radiographs should be obtained for areas where a fracture is suspected. Compression fractures of the spine can lead to increased BMD readings on DXA. If a compression fracture of the spine is suspected, an X-ray should be obtained. In patients with fractures, additional images may need to be obtained for surgical planning.

After therapy for osteoporosis is initiated, follow-up DXA scans are typically obtained every 2 years. Occasionally the DXA should be repeated within 1 year. There is no common clinical utility to checking a DXA scan more frequent than yearly. It is important to order this test only as clinically indicated to reduce unnecessary costs to the patient and the healthcare system.

7.4.3.3 Bone Biopsy

Bone biopsies are not routinely performed for the diagnosis of osteoporosis. They are not necessary for the diagnosis. There are two clinical utilities for bone biopsies during the workup of a patient

with suspected osteoporosis. One is to discover potential malignancy. The other is to distinguish between renal osteodystrophy and osteoporosis in patients with chronic kidney disease.

7.5 Treatment of Osteoporosis

The treatment of osteoporosis includes lifestyle modifications, supplements, medications, and fracture repair surgeries if necessary. Medical therapy typically is with bisphosphonate medications. Denosumab and anabolic agents such as teriparatide can also be used and should be in certain situations. Pharmacotherapy is indicated for patients with osteoporosis. Medications are also indicated for patients with osteopenia based on their FRAX score. The treatment threshold is a hip fracture risk of ≥3% over 10 years or a major osteoporotic fracture risk of ≥ to 20% over 10 years [25, 49].

7.5.1 Lifestyle Modifications

Lifestyle modifications for patients with osteoporosis should be undertaken in all patients with osteoporosis. Smoking increases fracture risk and smoking cessation decreases fracture risk [50]. Alcohol affects bone health as well. Although it is unclear exactly what the optimal daily intake of alcohol is, people who drink 0.5–1 drinks per day have a lower risk of hip fracture compared to those who abstain from alcohol or drink alcohol in excess [51]. Patients should be advised to drink less than three drinks per day for bone health. More stringent guidelines are recommended for various other health reasons.

Exercise is also important for bone health. All patients with osteoporosis, who do not have active fractures, should be advised to perform routine weight-bearing exercise. Weight-bearing exercise has long-term positive effects on BMD [52]. Counseling should include regular walking, strength training, and flexibility training. In general, patients should use low weights for weight training with the goal of multiple repetitions. Finally, exercising can help with balance and reduce fractures. In addition to exercise, patients should be encouraged to do safety evaluations on their homes and be counseled on fall precautions.

7.5.2 Calcium and Vitamin D

Calcium and vitamin D are important players in bone health. There is some evidence that calcium and vitamin D supplementation is beneficial to reduce fractures [53]. The data are not convincing, however, and it has recently been suggested that calcium and vitamin D supplementation does not decrease fracture risk in patients with osteoporosis [54]. This is in all patients, not just patients with vitamin D deficiency. Vitamin D supplementation is typically safe at doses between 800 and 4000 international units, but calcium supplementation can increase risk of nephrolithiasis [54]. This is why calcium is recommended to be obtained through the diet rather than through supplementations. Vitamin D is recommended to be obtained through the diet, supplementation, and sunlight. A daily intake of 1200 mg of elemental calcium and 800 international units of vitamin D is recommended. The goal vitamin D level is controversial. The Endocrine Society and other professional societies recommend a goal of 30–50 ng/dL; however, the Institute of Medicine recommends a goal for 20–30 ng/dL [55, 56]. Vitamin D dosing is discussed in more detail in the osteomalacia chapter.

7.5.3 Bisphosphonates

Bisphosphonates are first-line therapy for postmenopausal women and men with osteoporosis [25, 49]. The mechanism of action is at the level of the osteoclasts. They inhibit bone resorption which leads to increased bone strength. There are a variety of options available in the USA. Treatment normally starts with an oral medication which can be administered daily,

weekly, or monthly. Intravenous options are also available. Bisphosphonates are indicated for all patients who meet the criteria for pharmacotherapy for osteoporosis, as listed above, unless they have a contraindication.

All bisphosphonates should be used with caution in patients with even mild kidney dysfunction and cannot be used in patients with moderate to severe kidney disease in general. Oral bisphosphonates cannot be used in patients with severe gastroesophageal reflux, a history of bariatric surgery, or a history of esophageal or gastric ulcers, but IV formulations are safe for these patients. Gastroesophageal reflux is the most common side effect of oral bisphosphonate therapy. Mild, flu-like symptoms are common after IV bisphosphonate administration. Rare, severe side effects are discussed later.

Prior to treatment, creatinine, vitamin D, and calcium should be collected. Bisphosphonates can cause hypocalcemia, and calcium supplementation may be needed during treatment, especially prior to IV infusion. Monitoring of therapy should be done with a DXA every 2 years and clinical evaluation at least yearly. Compliance with therapy is often low for oral bisphosphonates due to side effects and difficulty with dosing. Clinical follow-up should be focused on determining compliance and evaluating for fractures. In general, a low trauma fracture is considered treatment failure. A review of available formulations in the USA is discussed next.

7.5.3.1 Alendronate

Alendronate is an oral bisphosphonate. Multiple clinical trials have shown the benefit of alendronate to improve BMD and decrease fracture rates [57]. It is dosed 10 mg daily or, more commonly, 70 mg weekly for osteoporosis. Osteoporosis prevention dosing is 5 mg daily or 35 mg weekly. It can also be used to prevent osteoporosis in patients on chronic glucocorticoid therapy at 5–10 mg daily. It cannot be used in patients with creatinine clearance less than 35 mL/minute. Alendronate must be taken on an empty stomach with water only. Patients must stay upright for at least 30 minutes after taking alendronate.

7.5.3.2 Risedronate

Risedronate is another oral bisphosphonate. It has also been shown to reduce fractures and increase BMD in multiple clinical trials [58]. For postmenopausal women, dosing for prevention or treatment of osteoporosis is 5 mg daily, 35 mg weekly, or 150 mg monthly. For men, the dosing is 35 mg weekly, and for patients on glucocorticoid therapy, the dose is 5 mg daily for prevention and treatment. It must be administered the same as alendronate. There are the same restrictions and common side effects as alendronate as well.

7.5.3.3 Zoledronic Acid

Zoledronic acid (zoledronate) is an IV bisphosphonate. It increases bone density and can reduce fracture risk by as much as 70% in the spine and around 40% in the hip in postmenopausal women [59]. It is dosed at 5 mg yearly for postmenopausal women and men with osteoporosis and for patients on glucocorticoid therapy for prevention and treatment. The does is 5 mg every 2 years for prevention of osteoporosis in other clinical settings. Zoledronic acid must be dose adjusted if creatinine clearance is ≤60 mL/minute and is contraindicated with a creatinine clearance <30 mL/minute.

7.5.3.4 Ibandronate

Ibandronate is an oral or IV bisphosphonate. Multiple trials have shown the efficacy of ibandronate to increase BMD and decrease fracture rates [60]. It is dosed either at 150 mg by mouth monthly or 3 mg IV every 3 months for postmenopausal women with osteoporosis. The preventative dose for postmenopausal women is also 150 mg by mouth monthly. Ibandronate oral dosing must be administered the same as alendronate and risedronate. It should not be used if creatinine clearance is <30 mL/minute.

7.5.3.5 Serious Bisphosphonate Adverse Reactions

Bisphosphonate therapy prevents far more fractures than the rare severe complications they cause [61]. Despite this, many clinicians and

patients are hesitant to start bisphosphonate therapy in patients with osteoporosis. Chief among concerns are atypical fractures of the femur and osteonecrosis of the jaw. Although these complications are rare, they can be clinically devastating.

7.5.3.6 Atypical Femur Fractures

Atypical femur fractures are low trauma fractures that can occur in patients with and without osteoporosis. Criteria for the diagnosis of atypical femur fractures have been defined by the American Society for Bone and Mineral Research and must include all major factors which include the following [62]:

1. No or minimal trauma
2. Subtrochanteric or femoral shaft location
3. Transverse or short oblique configuration that is noncomminuted with a medial cortical spike

Minor features may or may not be present and include [62]:

1. History of pain in the groin or thigh and a history of bisphosphonate or steroid use
2. Bilateral location
3. Localized periosteal reaction of the lateral cortex with generalized cortical thickening and/or sings of delayed healing

The rate of these fractures is not well known, but observational studies have revealed a probable stability in patients in the USA from 1996 to 2009 [63]. Patients with atypical femur fractures were more likely to be on bisphosphonate therapy and have osteoporosis. The highest risk appears to be with glucocorticoid use [63]. Patients appear to be at risk only after longer courses of bisphosphonate therapy. This has led to the recommendation to consider a drug holiday after 5 years of oral bisphosphonate therapy or after 3 years of IV bisphosphonate therapy [61]. The risk-benefit ratio of fracture prevention compared to atypical fractures strongly favors fracture prevention in patients with osteoporosis [61]. Future studies should focus on specific causes of these fractures which could further help determine treatment duration of bisphosphonate therapy.

7.5.3.7 Jaw Osteonecrosis

Jaw osteonecrosis is characterized by progressive bone destruction in the maxillofacial region. It typically happens after invasive dental procedures or after oral surgery. Bisphosphonate therapy has been linked to this as well as other antiresorptives including denosumab [64]. This rare side effect has been seen with oral and IV bisphosphonate. They occur in less than 1% of patients taking bisphosphonates for osteoporosis [64]. Rates of jaw osteonecrosis are much higher in patients receiving therapy for hypercalcemia of malignancy or bone metastasis. Risk appears to be dose dependent [64]. Dental consultation prior to starting bisphosphonate therapy has been shown to decrease jaw osteonecrosis and should be requested in patients with concerning findings on the physical exam prior to starting therapy [65]. As for atypical femur fractures, the number of fractures prevented far outweighs the risk of jaw osteonecrosis caused by bisphosphonates or other antiresorptive medications in patients with osteoporosis.

7.5.4 Denosumab

Denosumab is a human monoclonal antibody used for the treatment of osteoporosis. It inhibits RANKL which decreases osteoclast differentiation. This leads to decreased resorption of bone and increased BMD. Multiple clinical trials have shown that denosumab reduces fracture risk and increases BMD for patients with osteoporosis [66]. It appears that denosumab may increase BMD more effectively than some bisphosphonates, but it has not been clearly shown to reduce the fracture rate further [67].

Denosumab is approved for osteoporosis in men and women. It is also used for glucocorticoid, aromatase inhibitor, and androgen deprivation-induced osteoporosis. For all these indications,

dosing is 60 mg subcutaneously every 6 months. Unlike bisphosphonates, denosumab can be used in patients with chronic kidney disease including end stage renal disease. In patients with end stage renal disease, tetracycline-labeled bone biopsy should be used to confirm osteoporosis prior to starting therapy as denosumab would not likely be an effective treatment for adynamic bone disease associated with chronic kidney disease.

The duration of denosumab therapy is not well defined. One of the major problems with denosumab is that discontinuation of therapy leads to a rapid decline in bone density [68]. This is much different from bisphosphonate therapy, which continues to have a positive effect for years after therapy is stopped. Due to the concern of increased fractures, particularly in the spine, bisphosphonate therapy should be started after denosumab is discontinued for most patients.

In general, denosumab is well tolerated with no major side effects [66]. As denosumab is a monoclonal antibody to RANKL, there is a theoretical increased risk of infection. Minor and serious infections have been reported, but serious infections have not been linked clearly to denosumab [69]. The most common infection is a self-limited upper respiratory infection. There is evidence suggesting denosumab is safe for patients after organ transplant and with rheumatoid arthritis on immunosuppressants [70, 71]. Denosumab is an antiresorptive and therefore can cause jaw osteonecrosis as well as atypical femur fractures. Atypical femur fracture rate is not clearly defined and is a controversial potential adverse reaction. Osteonecrosis of the jaw occurs in less than 1% of patients on denosumab and is less frequent than in patients on bisphosphonates [64].

Denosumab is a good treatment option for osteoporosis. It is well tolerated with benefits outweighing risks for most patients. It is given as a 60 mg subcutaneous injection every 6 months. Due to increased fracture rates after discontinuation, therapy should be followed by bisphosphonate if denosumab is stopped.

7.5.5 Teriparatide and Abaloparatide

Teriparatide and abaloparatide are a PTH and a parathyroid hormone-related peptide (PTHrP) analog, respectively. Unlike other agents for osteoporosis previously described in this chapter, they are anabolic agents rather than antiresorptive agents. Teriparatide is PTH 1–34 which is a recombinant human parathyroid. It has the biologic activity of PTH. Abaloparatide is PTHrP 1–34 which is a synthetic analog [72].

Chronic exposure to PTH and PTHrP causes hypercalcemia and increased bone resorption compared to bone formation. This is through regulation of calcium, phosphorus, and vitamin D. Patients with prolonged exposure to excess PTH and PTHrP have increased risk for osteoporosis. Intermittent exposure causes dramatically increased bone formation without excess resorption, which can strengthen bones and reduce fracture risk [72]. Multiple clinical trials have shown this [72, 73].

Teriparatide is a subcutaneous injection dosed 20 mcg daily. It can be used for postmenopausal osteoporosis, male osteoporosis, and steroid-induced osteoporosis. Therapy is indicated for patients with severe osteoporosis or for people who fail antiresorptive therapy. It can also be used during drug holidays for patients previously on bisphosphonates [74]. Patient should only receive teriparatide for 2 years due to the potential risk of osteosarcoma. Bone density quickly declines after teriparatide is discontinued. An antiresorptive agent is therefore required after discontinuation of teriparatide [74].

Abaloparatide is a subcutaneous injection dosed 80 mcg per day. It is currently only approved for postmenopausal osteoporosis. Additional uses will likely soon be approved. It also should only be used for 2 years due to the potential risk of osteosarcoma and needs to be followed by an antiresorptive agent.

The risk of osteosarcoma is not known for patients on abaloparatide or teriparatide.

Perceived risk is due to rat studies which revealed a dose-dependent risk for osteosarcoma with both teriparatide and abaloparatide. No confirmed cases exist that link these drugs definitively with the condition [73, 75]. With current therapy guidelines recommending 2 years of therapy only, the risk is likely low.

Hypercalcemia is the most common risk with these drugs. Patients should not be supplemented with calcium while taking these medications. Hypercalcemia and hyperparathyroidism prior to therapy are contraindications to therapy. As these drugs are not antiresorptive agents, atypical femur fractures and jaw osteonecrosis are not concerns during therapy. The primary difficulty with using these medications is cost. It is also very important that patients not be lost to follow-up as fracture risk increases after stopping therapy. In general, these medications are well tolerated and an exciting treatment option for patients with osteoporosis.

7.5.6 Selective Estrogen Receptor Modulators

Selective estrogen receptor modulators (SERMs) are typically used for the treatment of breast cancer. They bind to selective estrogen receptors, and, therefore, do not carry the same risks of estrogen therapy. The SERM typically used is raloxifene. It has been shown to increase bone density and decrease vertebral fracture risk. Breast cancer rates are reduced in patients taking raloxifene as well [76]. Unfortunately, thromboembolic risk is increased with SERMs, and their effect on bone density is not as profound as the previously mentioned agents. They may be useful in select postmenopausal women, but they are not the best first-line therapies.

7.5.7 Estrogen Therapy

Estrogen therapy is no longer used regularly for postmenopausal osteoporosis. This is due to the risk of breast cancer, stroke, and venous thromboembolism in postmenopausal women taking estrogen therapy [77]. Estrogen can increase BMD however, and is often used after oophorectomy to maintain normal estrogen levels in premenopausal women. Premenopausal women with estrogen deficiency leading to low bone density should also be placed on estrogen therapy in most cases.

7.5.8 Special Populations

There are multiple special populations in which low bone density or osteoporosis should be considered differently than in postmenopausal women. For young people with low bone density, long-term treatment safety data is not available. There are several complications related to long-term therapies with the above-listed agents, which can make them poor choices for patients who may need treatment for more than 10 years. Other populations should be treated differently based on their bone disease or other clinical factors. Some of these populations are discussed further below.

7.5.8.1 Premenopausal Women

Premenopausal women may have low bone density for a variety of causes. In otherwise healthy women, low bone density is typically due to estrogen deficiency. This section will focus on women with estrogen deficiency and does not apply well to women on chronic glucocorticoid therapy.

Amenorrhea is a clinical clue that should raise concern for bone health in premenopausal women. Although not all amenorrhea is related to estrogen deficiency, it is a clinical presentation for many young estrogen-deficient women. A thorough workup should be undertaken with all amenorrhea patients. If low estrogen is discovered, then the underlying cause must be made clear. Excessive exercise and eating disorders leading to anorexia are fairly common problems in young women. This causes secondary estro-

gen deficiency and is often called hypothalamic amenorrhea. The diagnosis of osteoporosis is controversial in this group. Most agree that if a low trauma fracture occurs, the patient has osteoporosis, but before that, it is unclear when to diagnose.

Treatment is even more controversial. Whenever possible, the underlying cause should be addressed. Many of these women need a multidisciplinary approach to therapy with a mental health professional. Estrogen therapy should be used in the form of an oral combined contraceptive to help with bone health for most patients. Antiresorptive and anabolic agents discussed above should generally not be used. They may be safe for short-term use, but long-term safety is not known.

7.5.8.2 Patients with Chronic Kidney Disease

Patients with chronic kidney disease need a bone biopsy to prove they have osteoporosis and not another form of CKD-MBD. Once osteoporosis is proven, denosumab can be used [66]. Anabolic agents cannot be used in the setting of hyperparathyroidism or hypercalcemia. Many patients with chronic kidney disease have secondary hyperparathyroidism. Treating these patients can be challenging as they have multiple types of bone pathology. Bone disease related to chronic kidney disease is discussed further in other chapters.

7.5.8.3 Patients on Chronic Glucocorticoid Therapy

Patients taking chronic glucocorticoid therapy of more than or equal to 2.5 mg of prednisone or prednisone equivalent for 3 months or longer need special bone consideration. They often have low bone density and have increased risk of fracture. There are many osteoporosis medications approved for glucocorticoid-induced osteoporosis and include bisphosphonates, denosumab, and teriparatide. For patients on chronic glucocorticoid therapy, treatment is sometimes indicated to prevent osteoporosis as well.

The initial step is to risk stratify patients. Patients under 40 years of age are at high risk only if they had a previous low trauma fracture. They are at moderate risk with a Z-score ≤ -3 on DXA or with rapid bone loss. This is defined as 10% or more decline in BMD on DXA over a year. Patients under 40 years of age are also considered moderate risk if they are taking $\geq$7.5 mg of prednisone or prednisone equivalents daily for more than 6 months. If none of these requirements are met for high or moderate risk, then the patient is low risk [47]. For patients over 40 years of age, high-risk patients are those with a low trauma fracture history, those with T-scores ≤ -2.5 (men over 50 and postmenopausal women only), or those with a FRAX score indicating 10-year fracture risk of $\geq$20% for major osteoporotic fracture or $\geq$ 3% for hip fracture [47].

In patients over 40, a baseline DXA should be obtained within 6 months of starting glucocorticoid therapy. For patients less than 40 years of age, a DXA should be obtained in patients with history of fracture or other osteoporosis risk factors. In patients over 40 years of age, a FRAX assessment and DXA should be obtained in all patients [47]. If osteoporosis is discovered, then treatment should be started with pharmacotherapy.

All patients on chronic glucocorticoids should practice healthy lifestyle choices for their bones and have adequate vitamin D and calcium intake. In addition to patients with osteoporosis, patients at moderate to high risk for osteoporosis should also be treated with pharmacotherapy. This applies to adults over and under 40 years of age. Oral bisphosphonates are the preferred agents for prevention. Monitoring should include a yearly clinical assessment as well as DXA every 2–3 years in general [47].

Patients on glucocorticoid therapy with bone disease are challenging bone cases. It is important to monitor them for fracture and poor bone health. Treatment is indicated for those at moderate to high risk for fracture and for those with osteoporosis.

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Part II

Rheumatic Diseases

Rheumatoid Arthritis

8

Beth L. Jonas

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the key risk factors and concepts related to diagnosis and management of rheumatoid arthritis
- *Objectives*: On completion of this unit, the learner should be able to describe and define the:
  1. Risk factors for development of rheumatoid arthritis (RA)
  2. Pathophysiology and clinical presentation of RA
  3. Approach to diagnostic laboratory and imaging studies
  4. Principles of medical management in RA
  5. Role of surgical treatment

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8.1 Risk Factors

RA affects from 0.5 to 1% of the population worldwide, although it is reported to have a prevalence rate of 5% in some native American populations [1]. Risk factors for the disease include female gender, genetics, and certain environmental factors. Women are 2–3 times more likely to develop RA than men, and the reasons for this are not established. RA can occur at any age and the peak incidence is in the 60s.

Concordance for RA among monozygotic twins is reported to be about 10–15%. Genetic factors may be responsible for up to 60% of the risk for RA in patients who are ACPA positive [2]. HLA DRB1 is strongly implicated in both the onset of seropositive RA and the severity of the disease [3]. Disease-associated HLA DR alleles contain a common amino acid sequence in the binding groove of the molecule, the so-called shared epitope. This finding implicates an important role for peptide binding in the onset of the disease. Numerous other genes encoding immune and inflammatory pathways have also been associated with the development of RA, but these have a weaker association. It is likely that multiple risk alleles in association with environmental factors are important in the development of RA.

Among environmental factors, cigarette smoking is the most important. Smoking increases the risk of RA in a dose-dependent fashion, and it is most striking in RA patients who are positive for the CCP antibody or who have the shared epitope [4]. Current smoking is accompanied by increased levels of inflammatory mediators and increased disease activity. In addition, some studies have shown that smokers respond less well to disease-modifying therapy [5].

The microbiome has been implicated in the development of RA. Periodontal disease is associated with an increased risk of RA [6], and this is thought to be related to two oral pathogens, *Porphyromonas gingivalis* [7] and *Aggregatibacter actinomycetemcomitans.* The intestinal microbiota is also thought to possibly play a role in the development of RA [8].

8.2 Pathophysiology

The synovium plays a central role in the pathogenesis of RA. In its normal state, the synovium plays two important roles: to produce the lubricants necessary for the cartilage surfaces to effortlessly glide and to provide nutrients for the cartilage, which lacks its own blood supply. The hallmark of rheumatoid arthritis is synovial inflammation characterized by an expansion of synoviocytes which produce pro-inflammatory cytokines such as TNF-alpha, IL-6, and GM-CSF. In addition, there is infiltration of the synovium with mononuclear cells, predominantly CD4+ lymphocytes and macrophages. The synovial compartment becomes the nidus of inflammation with a complex interplay of cytokines, chemokines, matrix metalloproteinases, activated T and B cells, fibroblasts, and osteoclasts. Local inflammation in the synovium leads to the development of a pannus, a local tumor, mediating the destruction of cartilage and bone.

8.3 Clinical Presentation

8.3.1 Articular Features

RA is a symmetric inflammatory polyarthritis that can involve almost any joint. In early disease, the predominant joints are the small joints of the hands and feet, and over time other joints may become involved. Pain and swelling of the joints are the earliest sign of disease. This is often associated with morning stiffness or stiffness after any period of prolonged inactivity lasting several hours. Most patients describe improvement in stiffness and sometimes pain with activity. The joint swelling associated with RA is usually soft or boggy which can be differentiated from the joint swelling in osteoarthritis which tends to be more boney.

In the hands, the wrists, MCPs, and PIPs are typically involved with sparing of the DIPs. In the feet, involvement of the MTPs predominates. After the hands and feet, the most common joints involved are the elbows, shoulders, ankles, knees, and hip. As in the hands and feet, these joints become painful, stiff, and swollen.

On physical examination inflamed joints are tender, are swollen, and often have a reduced range of motion. When the hand joints are inflamed, the grip strength is diminished. A new diagnosis of carpal tunnel syndrome, particularly when bilateral, should raise the suspicion for RA since wrist synovitis can be a cause of a compressive median neuropathy. In the spine, RA is generally confined to the cervical region. Among the cervical spine joints the atlantoaxial (C1–2) joint is most prone to subluxation and may lead to a cervical myelopathy.

Over time, if the disease is not adequately treated, swelling and tenderness progress to articular damage with malalignment, subluxation, and dysfunction of the joints. In the hands this may manifest as ulnar deviation of the fingers at the MCP joints, swan neck deformities (extension of the PIPs with flexion of the DIPs), or boutonniere deformity (flexion of the PIP and extension of the DIPs). In the feet, erosive damage in the MTPs leads to lateral drift of the toes and plantar subluxation of the metatarsal heads leading to "cock-up" toes. Involvement of the midfoot is common and can lead to collapse with chronic tarsal malalignment and pain.

8.3.2 Extra-Articular Features

RA is a multisystem disease, and extra-articular features are a sign of more advanced disease and a poorer prognosis. The skin and eye are the most common organs involved aside from the joints. Subcutaneous nodules typically are found on the extensor surfaces of the forearm just distal to the elbow joint, but they can occur in many other locations including the dorsum of the hands and over the Achilles tendons. They can also be found in internal organs such as the lung, heart, and meninges. Rheumatoid nodules have a classical histology with a central area of necrosis surrounded by palisading macrophages and lymphocytes [9]. Up to one third of patients with RA have sicca or secondary Sjögren syndrome characterized by keratoconjunctivitis and/or xerostomia. Rarely, some patients may develop episcleritis or scleritis, the latter of which can be sight limiting.

Other organs that may be involved include the lungs (pleurisy and interstitial lung disease), the heart (pericarditis, premature atherosclerotic disease), the vasculature (small vessel vasculitis), and the nervous system (compressive neuropathies and mononeuritis due to vasculitis). Hematologic abnormalities are common including anemia of chronic inflammation and thrombocytosis. Patients with RA have an increased risk of hematologic malignancy compared to age- and gender-matched controls.

Patients with RA have a 1.5–2.0 times higher risk for cardiovascular disease when compared to the general population, and this risk is attributed to the role of chronic systemic inflammation [10]. While it is not clear whether control of inflammation can ameliorate this risk, strategies to control the known risk factors for cardiovascular disease as well as appropriate management of inflammation are recommended [11].

8.4 Laboratory Studies

Rheumatoid factor (RF) is present in about 75% of patients with RA, but in only about one half of patients with early disease. It is not specific for RA; it is seen in patients with mixed cryoglobulinemia, systemic lupus, and many viral illnesses. High-titer rheumatoid factor has a higher specificity for RA than a low titer, and higher titers are associated with a poorer prognosis. Antibodies to cyclic citrullinated peptides (CCP) are similarly insensitive for RA, but have a higher rate of specificity compared to RF [12]. The absence of a RF and/or CCP does not rule out the diagnosis of RA.

Synovial fluid evaluation shows an inflammatory joint fluid (>5000 cell/mm^3) with a predominance in polymorphonuclear leukocytes. Higher cell counts (>25,000 cells/mm^3) may occur and when they do should raise the suspicion of a joint infection. In that case, a synovial fluid culture should be obtained.

Markers of acute inflammation including the Westergren sedimentation rate and C-reactive protein are useful markers of disease activity in RA and can be used both to aid in diagnosis and

to follow disease activity in patients undergoing RA therapy. While markers of inflammation are typically elevated, the absence of this should not rule out the diagnosis of RA in the appropriate clinical setting.

Patients with active RA may have a mild to moderate normochromic normocytic anemia related to systemic inflammation. In addition, the platelet count may be mildly elevated. These values tend to normalize with effective treatment of the disease.

8.5 Imaging

8.5.1 Plain Radiographs

Plain radiographs of the hands and feet are recommended at baseline to assess any joint damage, although radiographs are frequently normal in early disease. Nonspecific signs of early inflammatory arthritis may include periarticular osteopenia and soft tissue swelling at this stage. As the disease progresses, there is loss of joint width signaling the loss of articular cartilage. Periarticular erosions occur later and can be seen at the ulnar styloid, base of the fifth metacarpal, and at the MCP and PIP joints. Later, ulnar deviation, subluxation, and other chronic deformities may become evident (Fig. 8.1). Routine periodic radiographic assessment is recommended to assure stability in patients undergoing therapy for RA. If radiographs show progression of disease despite therapy, this indicates a need for intensification of therapy.

8.5.2 Ultrasound

Ultrasonography is increasingly used in rheumatology practices to assess the degree of joint inflammation, the volume of synovitis, and the

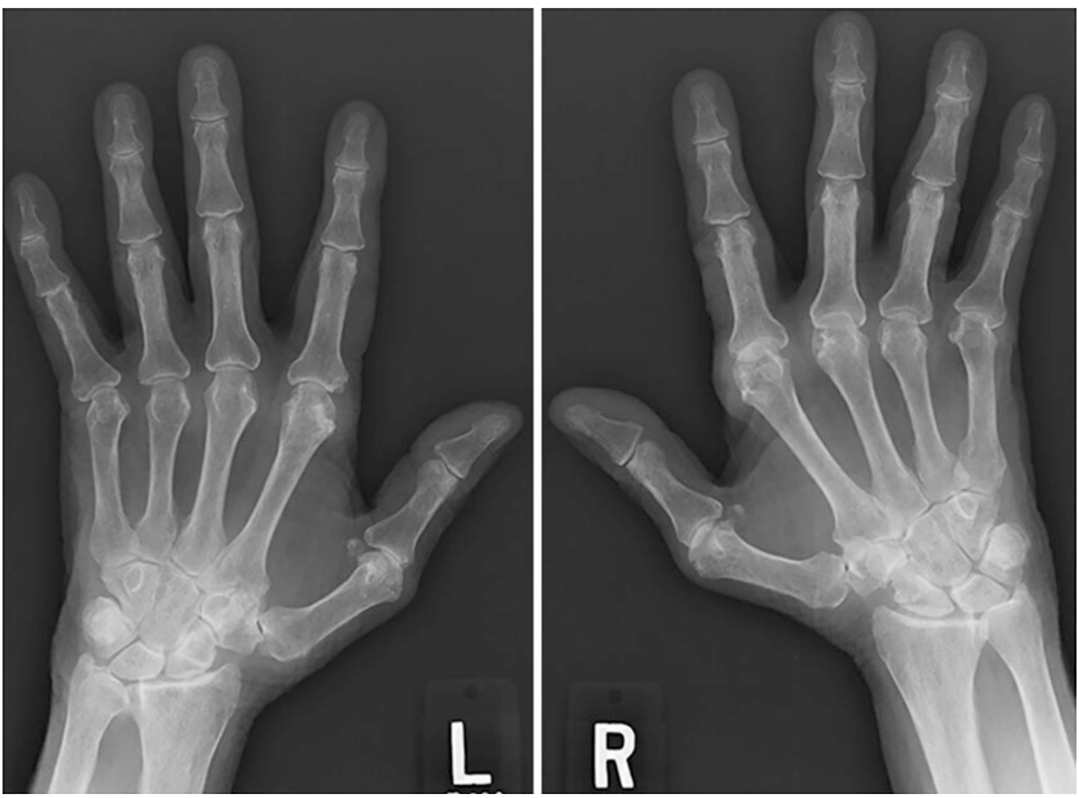

Fig. 8.1 Hand radiograph rheumatoid arthritis. There are diffuse osteopenia and soft tissue swelling noted around the MCP joints. There is joint space narrowing involving predominantly the MCP joints, radiocarpal joints, and scattered PIP joints with ulnar subluxation in the right hand. Numerous erosions involving the multiple bilateral MCP heads, left second proximal phalangeal base

presence of boney erosions. While plain radiography has been the standard imaging modality in RA, ultrasound has been shown to be more sensitive to change in boney erosion than plain radiography [13]. Ultrasonography may also be more sensitive than physical examination to assess subtle synovitis. Power Doppler ultrasound can be used to demonstrate active inflammation and can be used to monitor clinical response to DMARD therapy in patients with RA [14].

8.5.3 MRI

MRI is more sensitive in the detection of erosions than both plain radiography and ultrasound, but the clinical significance and natural history of these lesions are not known. Like ultrasound, MRI can also more accurately assess the volume of synovitis and intra-articular fluid than plain radiography [15]. In general, MRI is not regularly used to assess RA due to the need for MRI scanners appropriate for imaging the extremity, the uncertain clinical significance of the findings, and the cost of the procedure.

8.6 Diagnostic Approach

There are no diagnostic criteria for RA. The diagnosis of rheumatoid arthritis relies on a careful medical history and comprehensive physical examination with attention to the duration of symptoms, pattern of joint involvement, and complete assessment of other organ systems. Signs and symptoms of other autoimmune diseases should be queried including rash, oral ulcers, Raynaud phenomenon, infectious symptoms, alopecia, muscle weakness with elevated muscle enzymes, and antinuclear antibodies as these may indicate an alternative diagnosis.

The differential diagnosis is broad and includes other early autoimmune diseases such as systemic lupus, osteoarthritis, psoriatic arthritis, crystal-induced arthritis, and numerous viral diseases that can present with a symmetric polyarthritis. A symmetric polyarthritis may also be the initial presentation of a systemic vasculitis.

Table 8.1 ACR/EULAR classification criteria for rheumatoid arthritis

		Points
Joint involvement	1 large joint	0
	2–10 large joints	1
	1–3 small joints	2
	4–10 small joints	3
	>10 joints (with at least 1 small joint)	5
Serology	Negative RF and negative CCP	0
	Low-positive RF or CCP	2
	High-positive RF or CCP	3
Acute phase reactants	Normal CRP and WESR	0
	Abnormal CRP or WESR	1
Duration of symptoms	<6 weeks	0
	≥6 weeks	1

A score of ≥6/10 is needed for classification of a patient as having definite RA

In the correct clinical setting, a positive RF and/or CCP can be used to support the diagnosis of RA. Marginal erosive disease on plain radiographs of the hands and/or feet is also highly suggestive of RA in the appropriate clinical setting.

In many cases, a definitive diagnosis cannot be made on the first evaluation, and a provisional diagnosis of undifferentiated inflammatory arthritis may be made. It is best to leave the diagnosis open and assess the future evolution of the disease process before moving to a definitive diagnosis. In either the case of RA or an undifferentiated inflammatory arthritis, disease-modifying therapy will be indicated.

New classification criteria for rheumatoid arthritis were developed in 2010 by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) in collaboration [16] (Table 8.1). While these criteria can be used to support the diagnosis of RA, their primary goal is to define a homogeneous population for the purpose of clinical studies.

8.7 Treatment

8.7.1 Non-pharmacologic Management

The importance of lifestyle modification cannot be overemphasized. Smoking cessation is

strongly encouraged. Efforts to attain and maintain a healthy body weight are essential and should be supported with counseling on nutrition and appropriate exercise individualized to each patient. Physical activity has numerous positive effects in patients with RA including decreased disease activity, decreased pain and fatigue, improved quality of life, improved sleep, and lower rates of depression [17].

8.7.2 Pharmacologic Therapy

Once the diagnosis is established, disease-modifying therapy should be rapidly instituted (Table 8.2). Since therapeutic onset may take from weeks to months for DMARD therapy to become effective, initial treatment with either nonsteroidal anti-inflammatory medications or low-dose prednisone is recommended as a bridge. Low-dose 7.5–10 mg prednisone daily is generally adequate for most patients. Higher doses, while effective, will have a greater toxicity and may make tapering more difficult. NSAIDs should be avoided in patients with renal insufficiency, peptic ulcer disease, or other contraindications.

Table 8.2 Disease-modifying antirheumatic drugs for RA

Synthetic DMARDs
Hydroxychloroquine
Leflunomide
Methotrexate
Sulfasalazine
Targeted synthetic DMARDs
Baricitinib
Tofacitinib
Biologic DMARDs
TNF inhibitors
Adalimumab
Certolizumab
Golimumab
Infliximab
Etanercept
IL-6 receptor antagonists
Sarilumab
Tocilizumab
T-cell costimulation inhibitor
Abatacept
CD20 monoclonal antibody
Rituximab

Weekly low-dose oral or SQ methotrexate (MTX) is the first-line drug of choice for patients with RA [18] due to its high rate of efficacy and good long-term tolerability profile. Leflunomide is a good option as monotherapy for patients who are not able to tolerate methotrexate. Efficacy of therapy should be assessed at 8–12 weeks, and if it is not adequate to control the disease, therapy should be escalated. Combination therapy with an additional DMARD (hydroxychloroquine, sulfasalazine, leflunomide) or biologic, usually a TNF inhibitor, is recommended. Triple therapy with MTX, SSZ, and HCQ can be very effective in some patient populations who do not have an adequate response to MTX monotherapy [19].

When therapeutic changes are made, reassessment at around 12 weeks is important to make sure that treatment goals are being met. Tight control of disease is essential to prevent joint damage and maintain function [20]. Patients with the most severe disease will certainly require combination therapy and often frequent changes in biologic therapy to attain the optimal treatment response. Combinations of nonbiologic DMARDs and biologic DMARDs are more effective than monotherapy with either a nonbiologic or biologic DMARD [21]. Numerous biologic DMARDs with different mechanisms of action are available. In general, the efficacy of the biologic DMARDs is similar, and excellent treatment responses can be achieved with a wide variety of biologic DMARDs. Combinations of multiple biologic DMARDs are not recommended due to increase in toxicity.

Once a stable effective regimen of DMARDs is established, every effort should be made to taper off steroids and then decrease the NSAIDs to just prn use. Inability to withdraw steroids or NSAIDs indicates that the background DMARD therapy is not adequate and further adjustments to therapy are recommended.

8.7.3 Surgical Management

In general, surgical therapy is indicated only for disease that is resistant to medical therapy. The goal of surgery is to relieve pain and restore joint function [22]. Numerous surgical procedures are available to treat the manifestation of RA including tenosynovectomy for inflamed tendon sheaths or to repair tendon ruptures, synovectomy to remove inflamed synovium that is resistant to medical therapy, metatarsal head arthroplasties to relieve forefoot pain and improve walking, and joint fusion to stabilize painful destroyed joints. Total joint arthroplasty is reserved for patients with end-stage disease. The most common procedures include hip and knee arthroplasty, and in most cases the outcomes are very good. Other joints that may undergo total joint arthroplasty include the shoulder, elbow, and ankle.

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Osteoarthritis

9

Amanda E. Nelson

Contents

Goals and Objectives

- *Goal*: To provide the reader with an overview of the epidemiology, clinical features, and management of osteoarthritis (OA)
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe, discuss, or identify:

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1. The frequency of OA in the adult population and variation by key demographic factors
2. Common risk factors for OA
3. Key clinical features of OA, overall and by site of involvement
4. The role of diagnostic testing in OA
5. Principles in the management of OA, utilizing a combination of non-pharmacologic and pharmacologic modalities
6. Common comorbidities and consequences of OA

9.1 Epidemiology of Osteoarthritis

Arthritis affected more than 50 million adults in the United States (nearly a quarter of the adult population) in 2010–2012, and is estimated to affect more than 75 million in 2040 [1]. Even these large numbers are likely underestimates of the true burden of arthritis in the population [2]. Osteoarthritis (OA) is by far the most common form of arthritis, and as such is a major contributor to disability around the world [3]. The overall trends of increased age and obesity in the general population suggest that the impact of OA will continue to increase over time.

Table 9.1 ACR classification criteria for osteoarthritis of the hand, hip, and knee

Hand [4]	*Knee: clinical* [5]
1. Hand pain, aching, or stiffness on most days of prior month	1. Knee pain for most days of prior month
2. Hard tissue enlargement of ≥2 of 10* selected joints	2. Crepitus with active joint motion
3. Fewer than three swollen MCP joints	3. Morning stiffness lasting ≤30 minutes
4. Hard tissue enlargement of ≥2 DIP joints	4. Bony enlargement of the knee on examination
5. Deformity of ≥2 of 10* selected joints	5. Age ≥ 38 years
Diagnosis requires items 1–3 and either 4 or 5 10 selected joints = bilateral distal interphalangeal 2–3; proximal interphalangeal 2–3, and carpometacarpal joints	*Diagnosis requires 1 + 2 + 4, or 1 + 2 + 3 + 5, or 1 + 4 + 5*
	Knee: clinical and radiographic [5]
Hip: clinical and radiographic [6]	1. Knee pain for most days of prior month
1. Hip pain for most days of the prior month	2. Osteophytes at joint margins
2. ESR ≤20 mm/hours	3. Synovial fluid typical of osteoarthritis
3. Radiographic femoral and/or acetabular osteophytes	4. Age ≥ 40 years
4. Radiographic hip joint space narrowing	5. Morning stiffness lasting ≤30 minutes
Diagnosis requires 1 + 2 + 3, or 1 + 2 + 4, or 1 + 3 + 4	6. Crepitus with active joint motion
	Diagnosis requires 1 + 2, or 1 + 3 + 5 + 6, or 1 + 4 + 5 + 6

9.1.1 Classification Criteria

The American College of Rheumatology (ACR) classification criteria for hand, hip, and knee OA are shown in Table 9.1. While hand OA can be defined using only clinical criteria, classification of OA at the hip requires a combination of clinical and radiographic features, and knee OA can be defined using either clinical or clinical and radiographic features combined.

9.1.2 Definitions of Osteoarthritis

OA can be defined in a variety of ways, often with a combination of clinical and radiographic features. The definition used will have a significant impact on the estimated frequency of disease [7]. Radiographic OA usually requires the presence of an osteophyte (or bone spur), with or without joint space narrowing. Other features visible on radiographs include subchondral cysts

and sclerosis, indicative of bony changes. Clinical OA is often defined using the above ACR classification criteria and includes physical examination changes such as bony nodules or "nodes" in the hands, limited internal rotation of the hip, and crepitus with movement at the knee. Symptomatic OA reflects the combination of symptoms (such as pain, aching, or stiffness in and around the joint) in conjunction with radiographic evidence of OA. These features vary based on joint site, severity of disease or symptoms, and the duration of disease in addition to other factors.

9.1.3 Frequency of Osteoarthritis

This section provides an overview of prevalence estimates, given the variation expected based on definitions as described above, and also due to the population under study.

9.1.3.1 Radiographic Osteoarthritis

Radiographic knee OA, usually of the tibiofemoral joint, is present in up to 37% of US adults [8, 9]; patellofemoral knee OA is also common but is less well-studied, and is likely present in around a quarter of US adults [10]. Estimates for radiographic hip OA are even more variable based on population, from less than 1% up to nearly 30% [11]. Radiographic foot OA involving the first metatarsophalangeal joint is present in 12–35% of adults [12]. Radiographic OA of the hand and spinal facet joints is exceedingly common (>50%) but often asymptomatic.

9.1.3.2 Symptomatic Osteoarthritis

The prevalence of symptomatic OA is overall much lower than that of radiographic OA. The imperfect correlation between structure and symptoms in OA is well-known and a focus of ongoing study. Additionally, the presentation of symptoms can be affected by a number of other factors, including but not limited to race/ethnicity, sex, socioeconomic status, comorbid conditions, medications, centralized pain, access to care, and so on. As summarized by Lawrence et al., hand, knee, and hip symptomatic OA were present in 7%, 7–17%, and 9% of US adults, respectively [13].

9.1.3.3 Lifetime Risk of OA

Another way to consider the frequency of OA is to consider the lifetime risk of developing the disease. These models use data from longitudinal cohorts to estimate the likelihood of developing a condition over the lifespan (here, by age 85 years). In a large community-based cohort, the lifetime risk of developing symptomatic hand OA in at least one hand by age 85 was about 40%, and was greater for women, whites, and those with obesity [14]. Using similar methods, the lifetime risk of knee OA was 45%, and was higher for those with a history of knee injury and those who were obese [15]. For hip OA, the risk was lower at 25%, and no differences were seen among demographic groups [16].

9.2 Risk Factors and Etiology

OA was historically considered either an avoidable consequence of aging or a "wear-and-tear" degenerative condition affecting the cartilage. Neither of these is true. Instead, OA is a complex and heterogeneous disorder that can affect any moveable joint and results in numerous changes, from gross to molecular, within the joints including cartilage breakdown, bone remodeling, inflammation, and eventual loss of normal joint function. OA also has effects on the meniscus, synovium, tendons, ligaments, and muscle in and around the joints. OA has been termed "primary" in the absence of an injury history or other joint disease, and "secondary" in the presence of a clear predisposing condition [5]. However, an increasing number of local risk factors (such as femoroacetabular impingement morphologies at the hip and malalignment at the knee) and recognition of other predisposing factors such as genetics make this division less clear. There is a movement toward understanding these predisposing features as subgroups, or phenotypes, of OA, which may have very different pathophysiology and require more focused management [17].

There are a number of recognized risk factors for OA, and many of these are not modifiable, such as age, sex, race/ethnicity, and genetics [18]. Most notably, OA is an age-related condition, although it is not a universal consequence of aging as is sometimes thought [19]. OA is generally more frequent among women compared with men, with some exceptions. The site and severity of OA differ by race/ethnicity; for example, African Americans tend to have more large joint involvement but less hand OA compared with whites [20], while Chinese women have more knee OA but less hip and hand OA compared with whites [21]. Genetics also play a role, as OA has a substantial heritable component, and a number of genes have been implicated to date, although none of particularly high impact [22].

Other risk factors are potentially modifiable, that is, they may be amenable to interventions. The strongest risk factor affecting the greatest number of people is likely increased body mass index, or BMI. The strongest association is between increased BMI and knee OA [23], although modest associations have also been reported for hand and hip OA. Overweight and obesity likely act through two mechanisms, first by increasing load at weight-bearing joints and second by providing a pro-inflammatory milieu as evidenced by associations between metabolic syndrome and OA of various joints [24]. Nutritional and hormonal factors may play a role in OA as well, although evidence is mixed.

Local factors influence OA risk at a given joint. Foremost among these is varus malalignment of the knee ("bowlegged") which is strongly associated with medial knee OA incidence and progression [25]. Valgus ("knock-kneed") malalignment contributes to lateral knee OA although this is overall less common [26]. Others include variations in joint and bone shape, such as those associated with femoroacetabular impingement and developmental dysplasia at the hip [27]. Joint injury is a local insult that can lead to accelerated "post-traumatic" OA, such as that seen following anterior cruciate ligament tears, in young active individuals [28]. While physical activity in general is beneficial to joint health and a key component of OA management, heavy activity due to sport or occupational activities may be detrimental [29, 30]. Muscle weakness may be due to OA itself, or in some cases may be a predisposing factor [31].

9.3 Pathophysiology

The pathophysiology of OA is complex and only briefly summarized here. As already mentioned, OA is a disease of the whole joint, and pathologic changes can be identified in many different tissues. Cartilage, once thought to be the only or primary abnormality in OA, undergoes substantial changes in both matrix (fibrillation, fissuring, fragmentation, and expansion of calcified cartilage) and cellular (chondrocyte function and number) components, leading over time to increased vascularization, new bone formation, and degradation of mechanical properties [32]. The material properties of subchondral bone are also affected by changes including alterations in trabecular bone architecture, cyst, and osteophyte formation in OA. Bone marrow lesions, often noted on MRI, are associated with pain, and represent areas of bone remodeling and fat necrosis [33]. The synovium is also inflamed (termed "synovitis") in OA, although not to the extent seen in rheumatoid arthritis, a process driven by the alterations in cartilage and chondrocytes; synovitis is also associated with increased pain in OA [32].

9.4 Clinical Features

9.4.1 General

OA is most frequently seen in the knees, hands, feet, hips, and spine. The pain in OA tends to be worse with activity, with mild or no morning stiffness (less than 30 minutes), and pain and stiffness often noted at the end of the day. This is in contrast to more inflammatory arthropathies such as rheumatoid arthritis where the stiffness is often an hour or more and the pain tends to improve with activity, and to be most notable in the morning. On physical examination, a joint

affected by OA often exhibits bony enlargement and/or crepitus, which can be accompanied by reduced range of motion. While some soft tissue swelling may be present, it tends to be mild. As discussed earlier, OA symptoms are only partly due to structural damage as numerous other factors such as central sensitization, depression, and disturbed sleep also play a large role.

9.4.2 Joint-Specific

9.4.2.1 Knee

Knee osteoarthritis often presents as slowly progressive knee pain with limited range of motion, although it can sometimes present acutely with pain and swelling. The pain is generally most severe with weight-bearing activity, transferring from seated to standing, and with using stairs, and can be accompanied by a sensation of "give way" or locking. On examination, there is often tenderness at the medial and/or lateral joint line(s), but this can be more generalized. When effusion is present, it is generally cool and without redness; when large these can be associated with a popliteal cyst (Baker's cyst; see Fig. 9.2) and posterior pain. Varus malalignment is common and can be marked in severe disease.

9.4.2.2 Hip

Hip pain is often difficult for patients to localize, and pain due to hip OA can be variably described as groin pain (more specific), thigh or buttock pain, low back pain, or even ipsilateral knee pain. Other causes of pain in these areas, such as disc disease, facet OA, trochanteric bursitis, or even fracture, should be considered. When present, hip OA can lead to limitations in weight-bearing activities similar to the knee but may specifically affect internal rotation as demonstrated by difficulty tying shoes or putting on socks.

9.4.2.3 Hand

Bony enlargement at the distal interphalangeal (DIP) joints, termed "Heberden's nodes," or the proximal interphalangeal (PIP), or "Bouchard's nodes," may be the first indicator of a diagnosis of OA on exam. Bilateral involvement of multiple joints and joint groups (e.g., DIP, PIP, carpometacarpal [CMC]) is common. At times, these bony nodules can become inflamed with warmth and tenderness, and distinction must be made between the process of OA itself and other potential diagnoses (e.g., calcium pyrophosphate deposition disease, psoriatic arthritis). Erosive, or inflammatory, OA, generally seen in older women, is characterized by more inflammatory findings on exam and more damage on imaging, including central, or "gull-wing" erosions. It is unclear whether this condition is a separate entity or represents more severe OA [34]. First CMC OA can present with squaring due to joint deformity and is often a source of pain and functional limitation [35]. Prominent metacarpophalangeal (MCP) joint involvement can be seen in OA, but should also raise concern for other potential etiologies, such as crystalline arthritis or hemochromatosis [36].

9.4.2.4 Other Sites

The above are some of the most common sites affected by OA, but, particularly in the setting of prior injury, OA can be seen in almost any joint site. Facet joint OA is common and may contribute to back pain. Similarly, lumbar disc degeneration is often seen in the setting of OA, but the relationship of these two conditions is controversial. Shoulder pain, when due to OA, is most often in the acromioclavicular and/or sternoclavicular joints, but infrequently can involve the glenohumeral joint itself. The first metatarsophalangeal (MTP) joint in the foot is commonly affected by OA leading to hallux valgus (bunion) deformity and pain with ambulation. Ankle and elbow OA are relatively infrequent and usually seen in the setting of prior injury or crystal arthritis. Temporomandibular OA is more well-studied in the dental literature but can present with the same symptoms (e.g., pain, clicking, locking, crepitus) as OA in other joint sites.

9.4.2.5 Multi-Joint

Despite widespread use, there is no standard definition of "generalized OA," a term often used to describe the frequent finding of multiple joint involvement in OA [37]. In the clinical setting, the key is to recognize that a patient with OA in one joint is likely to have similar problems in other joints, and to assess the overall burden of disease in that patient. Awareness of multiple joint involvement in OA is useful for the patient's education, preventive and mitigating strategies, and prevention of functional decline beyond management of a single index or presenting joint.

9.5 Diagnostic Testing

In most cases, laboratory testing is not required as OA is primarily a clinical diagnosis. The utility of diagnostic testing is in excluding other potential arthritides, such as rheumatoid arthritis, psoriatic arthritis, and crystalline arthritis; other potential painful musculoskeletal conditions, such as osteonecrosis or fracture (particularly in the hip); or other mechanical disorders (which may or may not be related to OA in a given site).

9.5.1 Laboratory Testing

In general, there is no indication for serologic testing in clinically suspected OA. In cases where there are findings suggestive of a potentially more inflammatory process, such testing could be considered (e.g., more MCP involvement than expected and a family history of rheumatoid arthritis, or systemic findings suggestive of another process). Prior to considering pharmacologic treatment for OA (discussed below), especially in older patients or those with comorbid medical conditions, some tests, such as a complete blood cell count, chemistry panel, and liver function, are warranted. Although synovial fluid is not usually needed for diagnosis, if obtained during the course of the evaluation and/or treatment, it is generally normal to only mildly inflammatory (<2000 cells/mm^3). Calcium pyrophosphate crystals can be seen, but basic calcium crystals, or hydroxyapatite, cannot be visualized without specialized staining.

9.5.2 Imaging Findings

As noted above for laboratory testing, in many cases of clinically diagnosed OA, no imaging is needed. For clinically suspected hip OA, radiographs are useful to exclude other causes and can help to localize the pain to the hip joint. When indicated, conventional radiography is usually sufficient, and more advanced imaging modalities should be reserved for complex or unusual presentations or for research purposes.

9.5.2.1 Conventional Radiography

In settings of diagnostic uncertainty in OA, conventional radiography is an accessible and relatively inexpensive method to confirm the diagnosis. Radiographic features in OA include osteophytes (bone spurs), joint space narrowing (cartilage loss), subchondral sclerosis, and cysts. In a clinical setting, these features will be described qualitatively, whereas in a research setting, more standardized methods are needed. The semiquantitative Kellgren-Lawrence (KL) grading system [38] is the most commonly used, and ranges from a grade of 0 (no evidence of OA) to 4 (severe joint space narrowing with sclerosis; Fig. 9.1). A KL grade of 2 (definite osteophyte) is generally considered to represent a diagnosis of radiographic OA. Other semiquantitative grading systems are also used, particularly to separate individual radiographic features (e.g., osteophytes). More quantitative assessments, such as measured joint space width, can provide greater sensitivity to change over time compared with semiquantitative assessments, and can be efficiently performed with computer assistance [39].

At the knee, radiographs should be performed in weight-bearing, which provides a better assessment of the joint space. Pelvis radiographs to assess the hip joints can be supine or weight-bearing, and additional views (e.g., frog-leg or lateral) may be indicated for complete assessment. A posteroanterior image of

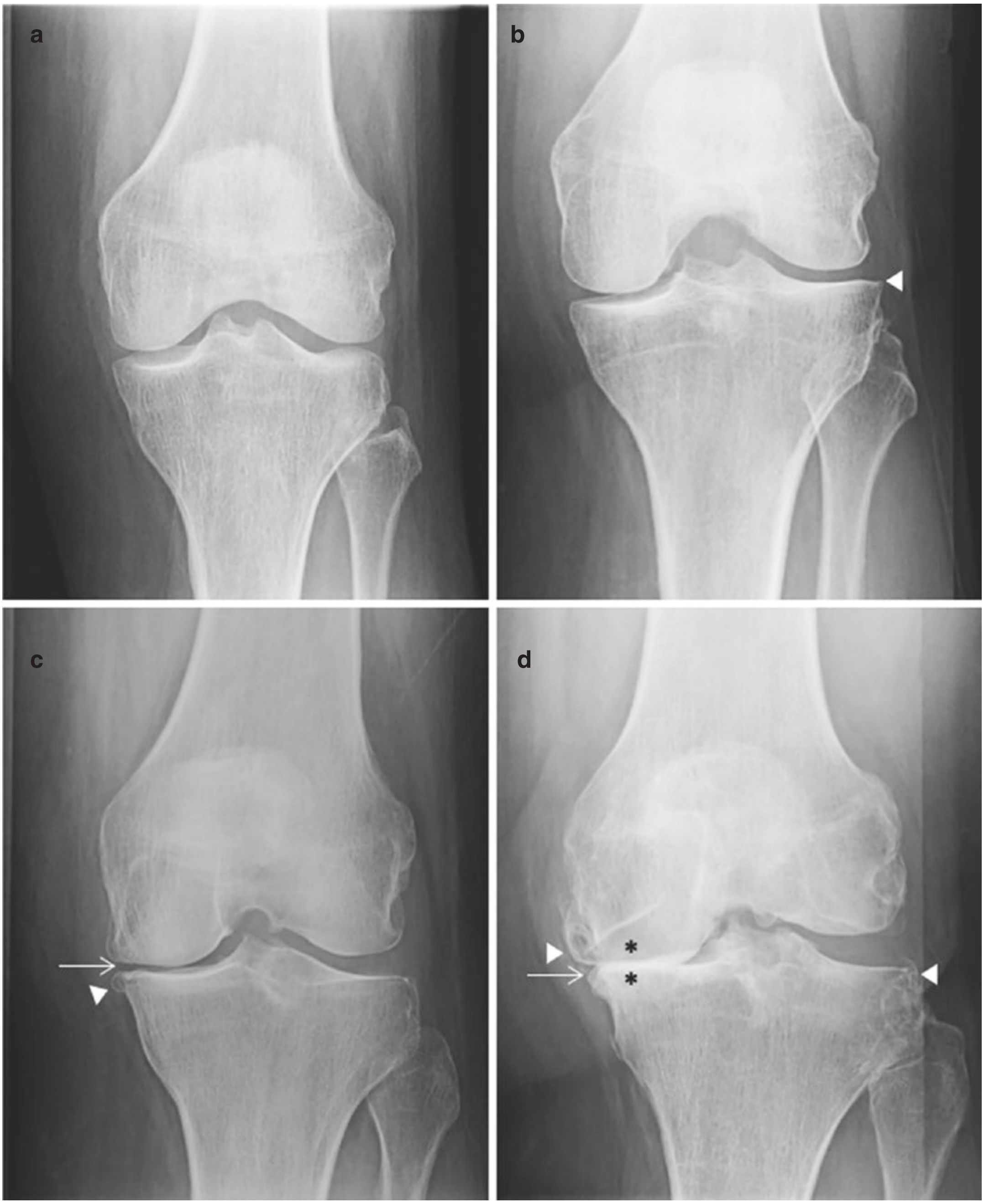

Fig. 9.1 Radiographic Kellgren-Lawrence grading (KLG) at the knee. (**a**) KLG = 0, normal, no evidence of osteoarthritis; (**b**) KLG = 1, small osteophyte of doubtful significance (arrowhead); (**c**) KLG = 3, definite osteophyte (arrowhead) with moderate joint space narrowing (arrow); (**d**) KLG = 4, osteophytes (arrowheads), severe medial joint space narrowing (arrow) and subchondral sclerosis (*)

both hands is sufficient to assess for hand OA, although again additional views may be needed in some circumstances. Due to overlapping structures, 2–3 views are needed to assess the foot joints for OA.

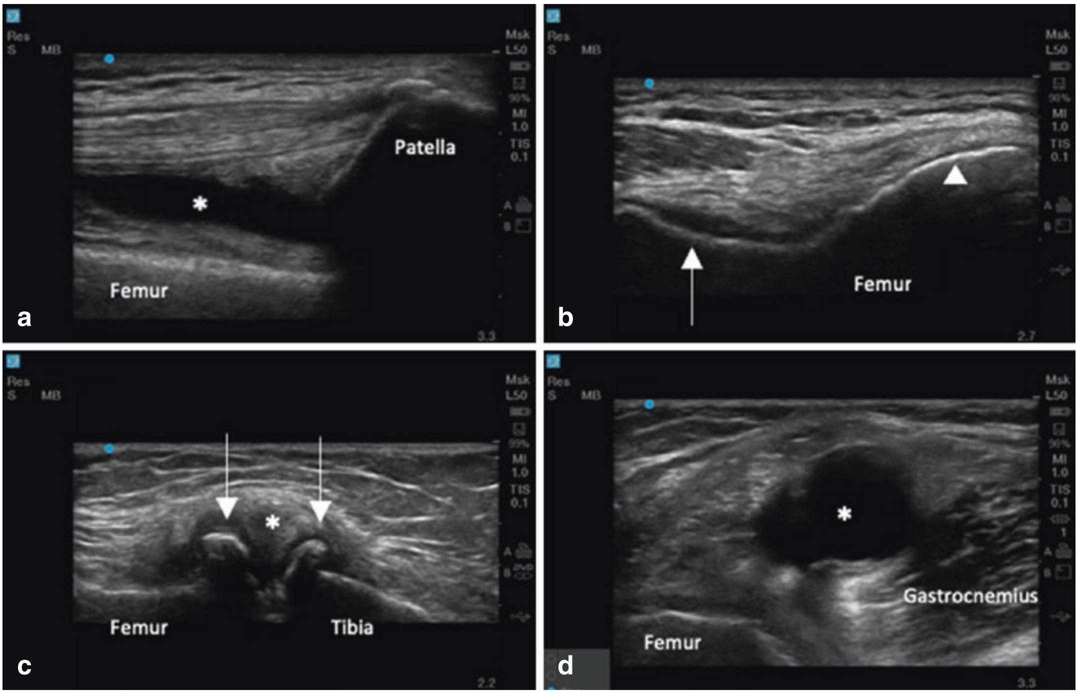

Fig. 9.2 Ultrasound images in knee osteoarthritis (by convention, the left side is proximal/medial). (**a**) Suprapatellar longitudinal view showing effusion (*). (**b**) Suprapatellar transverse in flexion showing moderate medial (arrow) and severe lateral (arrowhead) cartilage thinning. (**c**) Medial longitudinal with large osteophytes (arrows), meniscal extrusion is also seen (*). (**d**) Posterior transverse view demonstrating a popliteal cyst (*)

9.5.2.2 Magnetic Resonance Imaging

MRI is rarely indicated for clinically suspected OA, but it is increasingly used for research purposes because of its ability to provide detailed information about the non-osseous structures that are affected by OA, such as the cartilage, meniscus, tendons, ligaments, joint capsule, and synovium, as well as more detailed images of the subchondral bone [40]. Research MRI can be scored using a variety of semiquantitative or quantitative assessments, which can be focused on one or more of these tissues, or summative across the joint. Several excellent reviews are available on this topic for interested readers [41, 42]. Compositional imaging techniques that not only allow visualization of the structure but also characterize biochemical properties of tissues are also being used in OA research [43].

9.5.2.3 Ultrasound

Ultrasound (US) is an increasingly available point-of-care modality that can provide much of the same information as MRI in a more accessible manner. US is generally more sensitive than conventional radiography or physical exam and is comparable to MRI for detection of important features of OA such as osteophytes and effusion (Fig. 9.2). Direct assessment of cartilage and meniscus is possible with ultrasound as with MRI, although US cannot penetrate the bony cortex to image subchondral bone features. US can also be used in the clinic to guide therapeutic aspirations and/or injection at a variety of joint sites [44].

9.6 Principles of Management

The management of OA should be individualized for each patient, recognizing their goals, their disease burden and other comorbid conditions, and their personal preferences. There is no cure for OA, nor are there treatments that have been shown to stop progression; however, proper management

of the condition can improve pain, function, and quality of life. There are many separate guidelines from a variety of specialty organizations that discuss OA management; these have been recently reviewed and summarized [45, 46].

9.6.1 Non-pharmacologic

The cornerstone of OA management is non-pharmacologic. Given that no pharmacologic agent can slow or stop progression, and acknowledging the potential side effects of these agents, it is essential to focus on lifestyle and behavioral modifications that have been shown to have a beneficial effect. These can be divided loosely into (1) education and self-management; (2) exercise and weight loss; (3) assistive devices; (4) alternative and complementary approaches; and (5) surgical interventions.

9.6.1.1 Education and Self-Management

Self-management, which includes promotion of self-care, is a focus of all OA guidelines, recognizing the importance of the individual in their own disease management. Education regarding not just management, but also the nature and prognosis of OA, is important to empower patients to manage their symptoms on an individual basis.

9.6.1.2 Exercise and Weight Loss

There is broad recognition that low-impact exercise is beneficial in OA, although the specific type of exercise can vary, and there is no specific one-size-fits-all program. Both water- and land-based activities are beneficial, with the choice being one of preference and tolerability. Weight loss in overweight persons, particularly those with symptomatic knee OA, can provide substantial benefits in pain and function [47].

9.6.1.3 Assistive Devices

There is less consensus regarding assistive devices, although walking aids (such as canes, crutches, walkers) are generally recommended as needed for knee and hip OA. Other devices, such as knee braces, heel wedges, or specialized footwear, may be useful in specific cases but should be appropriately designed and fitted and instruction provided by a knowledgeable provider (e.g., physical or occupational therapist). Reaching and gripping aids can be useful for hand OA.

9.6.1.4 Alternative and Complementary Approaches

Again, due to the lack of effective pharmacologic treatments, alternative therapies are popular among OA patients. Acupuncture, specifically for knee OA, has been studied and is recommended by some groups, as is Tai Chi. Thermal modalities (e.g., ice and heat application) is generally recommended. There is a lack of consensus regarding transcutaneous electrical nerve stimulation (TENS), and therapeutic ultrasound was generally not recommended.

9.6.1.5 Surgical Interventions

The main surgical intervention of clear benefit in OA is total joint replacement, or arthroplasty, at the hip and knee, although it is important to remember that not all patients have good outcomes [48]. Partial or unicompartmental replacement is not generally recommended. Arthroscopy with debridement has been shown to be ineffective in symptomatic knee OA and is not recommended for this condition [49].

9.6.2 Pharmacologic

It bears repeating that pharmacologic therapy in OA is directed toward management of symptoms and does not alter the underlying course of the disease process. These agents should be considered as adjunctive therapies to assist with tolerability and adherence to the more effective non-pharmacologic interventions noted above. Acetaminophen has traditionally been considered the first-line agent for OA given its relatively benign side effect profile, but with increasing evidence that the effect size is very small and the risks have likely been underestimated, this is beginning to change [50]. Topical nonsteroidal

anti-inflammatory drugs (NSAIDs) are widely recommended for hand and knee OA [51], and may be more effective than oral NSAIDs in these sites, but are not effective for deeper structures such as the hip or spine. Oral NSAIDs, although moderately effective for symptomatic management, are limited in their use due to increased risk for gastrointestinal (which can sometimes be mitigated through addition of a gastroprotective agent) and cardiovascular adverse events in this patient population. Tramadol is often recommended for refractory pain, particularly for individuals with contraindications to other medications or who are not surgical candidates. Opioids, however, are not generally recommended due to limited efficacy in this group and poor side effect profile [52]. Other agents that are sometimes recommended but remain controversial include glucosamine/chondroitin, duloxetine, diacerhein, and others.

9.6.2.1 Intra-articular Therapy

Intra-articular corticosteroids are generally recommended for hip and knee OA, although they have at best a temporary benefit. Such injections may be useful for some joints affected by hand OA as well, although consensus has not been reached. There remains substantial controversy around other intra-articular therapies such as hyaluronic acid preparations, platelet-rich plasma, and mesenchymal stem cell injections, such that none of these are currently standard of care [53].

9.7 Consequences and Comorbidities

Osteoarthritis has, to some extent, been overlooked in clinical care in favor of more "serious" or "life-threatening" conditions such as cardiovascular disease, diabetes, etc. However, as detailed in a recent paper by the Osteoarthritis Research Society International (OARSI [54]), "OA has all the hallmarks of a serious condition. It causes premature aging…loss of functioning…premature mortality…disability." The authors go on to state that "OA has has a significant impact on day-to-day functioning and…it has no known cure or spontaneous remission and is associated with irreversible structural damage and progression over time" [54]. The high prevalence of this condition has been discussed earlier in this text, which should highlight the importance of managing this common chronic condition in all care settings.

One in four US adults has more than two chronic conditions; in adults with OA, the majority have at least one other significant chronic condition (e.g., cardiovascular disease, diabetes, hypertension, lung disease) [54]. Around a third of patients with OA have five or more other chronic conditions, indicating a subset with a very high disease burden [55]. These conditions have important effects in an individual. For example, concomitant cardiovascular disease and hypertension make NSAID therapy relatively contraindicated for OA management. Individuals with any or all of these conditions benefit from physical activity, but joint pain may limit their ability to participate. Individuals with comorbidities generally have more pain, greater activity limitation, and poorer prognosis [54]. It is important to consider the burden of these conditions on an individual, and how interactions between these conditions may be impacting their management. Additionally, individuals with OA have greater mortality than those without [56], and are more likely to experience work limitation, withdrawal from the workforce, absenteeism, and presenteeism; this is necessarily associated with substantial economic losses (due to lost work-related income) and increased health utilization and costs [57].

9.8 Conclusion

Osteoarthritis is a highly prevalent condition with an increasing frequency given our aging population and the epidemic of obesity. Prompt diagnosis and individualized management of this disabling condition are key to reducing the potentially serious consequences of this common chronic disease.

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Seronegative Spondyloarthropathies

10

Ellen Amanda Snyder

Contents

Goals and Objectives

- *Goal*: To introduce the readers to the seronegative spondyloarthropathies
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Clinical symptoms associated with the seronegative spondyloarthropathies

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2. Physical exam findings commonly seen in seronegative spondyloarthropathy
3. Laboratory and imaging studies that support a diagnosis of seronegative spondyloarthropathy
4. Similarities and differences among the different forms of seronegative spondyloarthropathy
5. General treatment strategies of the seronegative spondyloarthropathies

10.1 Introduction

The seronegative spondyloarthropathies (SpAs) are a group of disorders including ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), psoriatic arthritis (PsA), inflammatory bowel disease (IBD)-associated arthritis, reactive arthritis, and juvenile-onset spondyloarthritis (JSpA). These disorders are termed seronegative due to the absence of rheumatoid factor (RF). While there is a great deal of clinical heterogeneity among these disorders, they share several characteristic musculoskeletal features including inflammatory back pain, asymmetric oligoarthritis, enthesitis, dactylitis, and an association with human leukocyte antigen (HLA)-B27 positivity [1, 2].

Members of the SpA family can be grouped into two categories according to the distribution of joint involvement. Axial SpA involves the axial skeleton and presents with spondylitis and sacroiliitis. This group includes AS and nr-axSpA. Psoriatic arthritis, IBD-associated arthritis, and reactive arthritis typically present with peripheral arthritis, enthesitis, and tenosynovitis and are thus classified as peripheral SpA. The distinction between axial and peripheral disease is used for classification in clinical trials and for guiding certain treatment decisions. However, it is important to recognize these categories do not represent distinct entities, and significant overlap in various clinical and laboratory features may occur [2–4].

10.2 Clinical Features

The distribution and character of musculoskeletal involvement, in addition to the association with certain non-musculoskeletal features, distinguish the seronegative SpA from other forms of arthritis.

10.2.1 Musculoskeletal Features

- Inflammatory back pain – Lower back pain is a prominent feature of the seronegative SpAs, particularly those with axial involvement. The most common presentation is that of inflammatory back pain associated with inflammation of the sacroiliac (SI) joints, also known as sacroiliitis. Inflammatory back pain exhibits several clinical features that are distinct from those of non-inflammatory (or mechanical) low back pain. Inflammatory back pain is characterized by a dull, aching pain of the lower back, buttocks, or hips that is of insidious onset and chronic duration (>3 months). Onset of these symptoms usually occurs before 45 years of age. This pain is typically worse in the early morning and is associated with morning stiffness lasting 30 minutes or more. Patients may also experience significant pain at night. Inflammatory back pain characteristically improves with movement and warm showers (or warm compress) and worsens with rest. Good response to treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) is another feature of inflammatory back pain [1, 4, 5].
- Peripheral arthritis – Arthritis affecting joints other than those of the axial skeleton is known as peripheral arthritis. The peripheral arthritis in seronegative SpA typically presents as a chronic, inflammatory oligoarthropathy, meaning only one to four joints are involved. Both large and small joints may be affected. Pattern of involvement is often asymmetric and preferentially involves joints of the lower extremities although any joint can be affected. Severity ranges from mild to severe and can lead to significant disability in some patients [6–8].

- Enthesitis, tenosynovitis, and dactylitis – Enthesitis, tenosynovitis, and dactylitis are features commonly observed in seronegative SpAs. Entheses are the sites where tendons, ligaments, and articular capsules attach to the bone. Inflammation of the entheses is known as enthesitis or enthesopathy. Common sites of enthesitis include the heel (calcanei), hip (greater trochanter), elbows (epicondyles), knees (tibial plateau), and ligaments involving surrounding the intervertebral discs [9, 10]. Inflammation of a tendon and its surrounding sheath is called tenosynovitis. Tenosynovitis involving the flexor tendons of the hands and feet, in addition to diffuse soft tissue swelling and synovitis within the joint spaces, contributes to the development of dactylitis – another characteristic feature of the seronegative SpA family. Dactylitis is sometimes referred to as "sausage" digit and presents as swelling of an entire finger or toe. Of the seronegative SpA, dactylitis is most often observed in psoriatic arthritis and reactive arthritis. Dactylitis is not a specific finding to the seronegative SpA as it can be observed in other conditions such as tuberculosis, sickle cell disease, sarcoidosis, and tophaceous gout [11–13].
- Other musculoskeletal manifestations – Several other musculoskeletal features may be observed in the seronegative SpA. These include decreased spinal mobility, poor posture (forward-leaning posture, dorsal kyphosis, etc.), and decreased chest wall expansion. While these manifestations are more often observed in patients with long-standing disease, they can develop at any time over the course of disease [13–15].

10.2.2 Non-musculoskeletal Features

- Ocular manifestations – Inflammatory eye disease is the hallmark ocular manifestation of seronegative SpA. Anterior uveitis (iritis) is the most common form of inflammatory eye disease and occurs in up to 40% patients with seronegative SpA. It has a high association with HLA-B27 positivity [16–18]. Although less commonly observed, posterior uveitis, panuveitis, scleritis, episcleritis, and conjunctivitis have all been described in association with seronegative SpA [17, 19, 20]. The initial presentation of anterior uveitis is typically acute in onset and unilateral in distribution. However, with time, both eyes can be involved – often with alternating patterns of symptoms. Symptoms include pain, ocular erythema, and photophobia. Importantly, uveitis may be the presenting feature of the seronegative SpA and should prompt physicians to consider a diagnosis of SpA, particularly in instances of recurrent uveitis [17, 20]. Symptoms typically respond to topical anti-inflammatories, but some cases may require treatment with systemic immunomodulatory medications.
- Gastrointestinal manifestations – The seronegative SpAs are associated with inflammation of the bowel mucosa. Some studies indicate that up to two-thirds of patients with SpA have histologically determined inflammatory lesions of the gut mucosa. These histologic lesions are often clinically silent but may be associated with symptomatic IBD [21, 22]. Likewise, SpA is the most common extraintestinal manifestation of IBD with an estimated prevalence of 17–39% [23, 24]. Patients with IBD may present with axial and/or peripheral arthritis. While SpA is associated with both forms of IBD, arthritic symptoms appear to be more common in Crohn's disease [25]. Importantly, there appears to be a link between inflammatory arthritis activity and gastrointestinal inflammation. Remission of joint inflammation has been associated with disappearance of gut inflammation, while persistence of inflammatory arthritis has been linked to persistent bowel inflammation [21, 22, 26].
- Skin and nail manifestations – Psoriasis is the most common skin disease associated with the seronegative SpA. While most commonly associated with psoriatic arthritis, psoriasis has been associated with all forms of SpA and can occur in up to 10% of patients with ankylosing spondylitis [18]. Nail changes can be observed in association with psoriasis and seronegative

SpA. Common findings include nail pitting, ridges, discoloration, and separation of the nail from the nail bed [27, 28].
- Cardiac manifestations – Patients with seronegative SpA, particularly those with AS, are at increased risk of several cardiac manifestations including diseases of the aortic root and aortic valve, conduction abnormalities, and acute coronary syndrome [29–32]. Aortic root disease and conduction abnormalities are suspected to be due to an inflammatory process that interferes with the structural and physiologic integrity of the aortic root, valve cusps, and interventricular septum. Aortic root disease can result in aortic valve insufficiency, dilatation of the ascending aorta, and, rarely, aortic dissection, which is the most concerning manifestation owing to the high morbidity and mortality of this condition [32, 33]. Several studies have demonstrated an increase in ischemic heart disease in patients with seronegative SpA when compared with the general population. As with other systemic rheumatic diseases, this increased risk has been attributed to the presence of ongoing systemic inflammation as well as the increased prevalence of traditional cardiovascular risk factors in these patients [29, 30, 34].

10.3 Physical Exam

Physical exam findings of the seronegative SpA may vary depending on which subtype is being evaluated. In general, a physical exam should be performed to evaluate for both musculoskeletal (axial and peripheral manifestations) and non-musculoskeletal features of the disease.

The peripheral skeleton should be evaluated for evidence of synovitis, tenosynovitis, and enthesitis with careful attention to distribution and pattern of involvement. When evaluating the axial skeleton, there are several special maneuvers that assist in assessing for disease. These are listed below:

- FABER testing is performed to assess SI joint pain. The test is performed with the patient in the supine position with one leg extended and the other flexed, abducted, and externally rotated (in a figure-4 position). Posterior position is applied to the ipsilateral knee. Pain localized to the SI joint suggests SI joint dysfunction and possible sacroiliitis [35, 36].
- Modified Schober test assesses range of motion (ROM) of the lumbar spine in flexion. To perform this test, the dimples of Venus must be identified. A mark is made 10 cm above the dimples of Venus, and a second mark is made 5 cm below (total 15 cm). The patient is asked to stand shoulder-width apart and bend forward to touch the ground while keeping the knees straight. The distance between the points should increase to 20 cm. Anything less suggests restriction in spinal ROM [37].
- Occiput-to-wall testing evaluates cervical extension. The patient is asked to stand with his or her back against the wall. The patient's heels and shoulders should be flushed against the wall. In this position, the occiput should touch the wall. If not, there is cervical spine pathology preventing normal ROM [38].
- Chest expansion testing is performed to evaluate rib mobility. Measurements are made at the fourth intercostal space during maximal inhalation and exhalation. Anything less than a 2.5 cm difference is considered abnormal [37].

Non-musculoskeletal system involvement should also be evaluated. A thorough cardiopulmonary exam is required to assess for aortic disease and valvular dysfunction as well as evidence of respiratory dysfunction (i.e., restrictive lung disease). Skin exam should be performed with careful attention to areas where rashes may hide (scalp, ears, gluteal cleft, etc.) to evaluate for psoriasis. Nail exam should be performed to look for any irregularities – this may require requesting the removal of false nails or nail polish. An examination of the head and neck to evaluate for ocular erythema (inflammatory eye disease) and/or oral ulcerations (IBD associated) is also strongly encouraged.

10.4 Laboratory Features

There are no specific laboratory findings associated with the seronegative SpA. Elevated acute phase reactants, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), may be observed in axial and peripheral SpA. In early axial SpA, elevated levels of CRP are a predictor of radiographic progression [39]. Elevated CRP levels also predict a good response to tumor necrosis factor (TNF)-blocker therapy [40]. HLA-B27 is the major gene determining susceptibility to the seronegative SpA [41]. HLA-B27 positivity is found in 80–95% of patients with AS depending on ethnicity. In other forms of SpA, HLA-B27 is positive in 50–70% of patients [42, 43]. Seronegative SpA patients with positive HLA-B27 tend to experience onset of symptoms at a younger age and have increased risk for involvement of the axial skeleton. It is important to note that a positive HLA-B27, alone, is not sufficient for diagnosis as the national prevalence of HLA-B27 in the USA is estimated to be around 6.1% and only a small percentage of these individuals go on to develop disease [43–45].

10.5 Imaging

10.5.1 Plain Radiographs

Plain radiographs of the axial and peripheral skeleton play a major role in the evaluation and diagnosis of seronegative SpA.

- Axial radiographs – Plain films of the axial skeleton can be used to evaluate for presence of sacroiliitis, syndesmophyte formation, and other changes of spondylitis in the spine. Standard AP films of the pelvis should be obtained to evaluate for changes of the SI joints. Normal SI joints exhibit a uniform joint width and well-defined thin white subchondral bony margins bilaterally. In disease, poor definition and/or loss of the white cortical line may begin on the iliac side of the SI joint. Predilection for early involvement of the iliac side is due to thinner cartilage on the iliac side in comparison with that on the sacral side of the joint. These early abnormalities can progress to more obvious erosions, changes in joint space width, and sclerosis. With progression of disease, the most obvious changes are large erosions and fusion of the SI joints [46, 47]. In general, SI joint abnormalities are typically graded from 0 (normal) to 4 (total ankylosis) to identify the nature and severity of involvement [48–50]. In AS, SI involvement is typically bilateral and symmetric. In the other seronegative SpA, SI involvement may be unilateral or bilateral (but tends to be more asymmetric) [46, 47, 50]. In the spine, plain radiographs of patients with seronegative SpA may reveal "shiny corners" and squaring of the vertebral bodies. Later in disease, the gradual ossification of the outer layer of the annulus fibrosis leads to formation of bony bridges between vertebrae known as syndesmophytes. With time, formation of syndesmophytes along the spine can result in fusion of the vertebral column, which gives the appearance of a "bamboo" spine [46, 51].
- Peripheral radiographs – Plain radiographs of the peripheral joints in seronegative SpA may demonstrate a myriad of radiographic findings including joint erosions, periostitis, new bone formation, and lysis of the terminal phalanges. The pencil-in-cup deformity, which arises from periarticular erosions and bone resorption, can be seen in some cases of psoriatic arthritis [52, 53]. Radiographs can also reveal fluffy periostitis and new bone formation at the sites of enthesitis. Another finding that may be seen is diffuse soft tissue swelling of an entire digit reflecting dactylitis [53].

10.5.2 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) may be a useful imaging modality in patients with suspected or diagnosed seronegative SpA but normal plain films. MRI is known to show inflammatory lesions and structural changes long before they appear on radiographs. As such, MRI of the SI joint is often obtained for early detec-

tion of inflammatory changes to aid in diagnosis and treatment of the seronegative SpA, particularly the nr-axSpA [49, 54–56] On MRI, the active inflammatory lesions of sacroiliitis appear as high-intensity bone marrow edema (BME) on short tau inversion recovery (STIR) and T2 with fat absorption images. Other inflammatory findings such as synovitis, enthesitis, and capsulitis in addition to structural changes including sclerosis, erosion, and bony ankylosis may also be seen on MRI [49, 55, 56].

10.6 Specific Forms of the Seronegative Spondyloarthropathies

10.6.1 Ankylosing Spondylitis

AS is the best characterized member of the seronegative SpA family. It primarily affects the axial skeleton with inflammatory back pain and progressive spinal stiffness as its major features. Prevalence estimates of AS vary depending on the ethnic community studied. In North America, mean prevalence of AS has been reported to be 31.9 per 10,000 [57]. There is a strong association between AS and the HLA-B27 haplotype with up to 95% of AS patients demonstrating HLA-B27 positivity. The disease typically manifests before the age of 40 and has a 3:1 male predominance [44, 58].

AS is distinguished from other members of the SpA family by the universal presence of sacroiliitis on plain radiographs. In comparison with other forms of SpA, spinal involvement is more significant. Spinal disease may result in fusion and impaired spinal mobility, which is associated with postural abnormalities, decreased chest expansion (with or without restrictive lung disease), vertebral fractures, and various neurologic manifestations [59–61]. Incidence of vertebral fractures in AS ranges from 4% to 18% with the lower cervical spine being the most common site of involvement [61–63]. Fractures often occur with relatively minor trauma, which can result in delayed diagnosis. Neurologic symptoms may arise from spinal cord or nerve root compression due to vertebral fracture and instability. As such, careful attention may be required for diagnosis, and patients should be counseled thoroughly regarding the risk of fracture [64].

In addition to the spine and SI joints, the hips and shoulders are commonly involved in AS with up to 50% of patients being affected [65, 66]. Interestingly, the presence of radiographic hip involvement in AS has been shown to be a marker of more severe disease [67]. Other peripheral joint involvement can occur but is less common than that of the hips and shoulders.

Non-musculoskeletal features include those described earlier in this chapter with cardiothoracic manifestations being most unique to AS. Certainly, routine cardiac evaluation is required to assess for aortic disease, valvular disease, and arrhythmias. Pulmonary evaluation may require pulmonary function tests to help identify underlying lung disease.

10.6.2 Non-radiographic Axial Spondyloarthropathy

The term nr-axSpA was first developed as part of the 2009 Assessment of SpondyloArthritis international Society (ASAS) classification criteria in an attempt to better identify and classify patients with early or atypical disease that previously fell under the "undifferentiated SpA" category. Like AS, nr-axSpA primarily affects the axial skeleton. However, unlike AS, there is no definite evidence of sacroiliitis on conventional radiography. Instead, sacroiliac inflammation is detected on MRI. As such, patients are diagnosed with nr-axSpA based on some combination of presenting symptoms, HLA-B27 positivity, and findings on MRI. It remains unclear whether AS and nr-axSpA represent different points along the same continuum of disease or if these entities are distinct disease processes altogether. Several studies support the former theory by reporting approximately 5–20% of patients with nr-axSpA will develop radiographic sacroiliitis over a period of 2–10 years after initial diagnosis [68–70]. There has been a great deal of interest in understanding the natural history of nr-axSpA with particular

interest in determining if the identification and treatment of nr-axSpA can prevent progression of disease and/or the development of AS. Currently, data is limited and treatment recommendations follow those of AS [71–73].

10.6.3 Psoriatic Arthritis

PsA is a seronegative inflammatory arthritis associated with psoriatic skin disease. The overall prevalence of PsA is estimated to be between 1 and 2 per 1000 in the general population with men and women equally affected [74, 75]. While not all patients with psoriasis have PsA, it is estimated that up to 30% of psoriatic patients will develop PsA at some point over the course of their disease. Most patients have evidence of active psoriatic skin diagnosis at the time of diagnosis. However, it is important to recognize inflammatory arthritis may precede skin disease in 10–15% of cases [76–78]. Moreover, undiagnosed psoriatic skin lesions are present in up to 15% of cases at the time of PsA diagnosis. If presence of psoriasis is not obvious on exam, close examination of the scalp, area behind the ears, umbilicus, and gluteal (natal) cleft is recommended as these are areas where psoriasis may hide. Although there is no association between presence of inflammatory arthritis and pattern of psoriasis (i.e., plaque, pustular, guttate, inverse), there are some reports that suggest PsA is more common in patients with widespread skin involvement [77, 78].

Patients with psoriatic arthritis present with both peripheral and axial diseases – although peripheral arthritis is more common. There are five major patterns of arthritis associated with psoriatic arthritis: (1) distal (DIP predominate) pattern, (2) asymmetric oligoarticular pattern, (3) symmetric polyarthritis ("rheumatoid-like") pattern, (4) arthritis mutilans (osteolysis and destructive arthritis) pattern, and (5) isolated axial (asymmetric sacroiliitis) pattern [79]. These patterns are not mutually exclusive and overlap does occur. Patients may also present with one pattern initially but change patterns over the course of the disease [80, 81]. Other musculoskeletal clinical manifestations commonly seen in psoriatic arthritis include enthesitis, tenosynovitis, and dactylitis. Nail changes are often seen in patients with PsA, and those with DIP involvement tend to have more extensive nail disease than those with other patterns of arthritis [82, 83].

Treatment of psoriasis and PsA requires a multidisciplinary approach with both rheumatologists and dermatologists contributing to the therapy plan. Systemic therapies (as discussed later in this chapter) may address skin and joint symptoms. In many cases, patients will also require topical treatments to help control certain skin manifestations. Psoriasis, and therefore PsA, is associated with several comorbid conditions including metabolic syndrome, hypertension, diabetes, and cardiovascular disease. Interestingly, the presence of both metabolic syndrome and diabetes in patients with PsA is associated with more severe skin and joint disease [84]. So, while it is important to identify and treat PsA, it is also important to recognize other related conditions that may be impacting the overall health of the individual.

10.6.4 IBD-Associated Arthritis

Inflammatory arthritis is one of the most frequently encountered extraintestinal manifestations of IBD with ulcerative colitis (UC) and Crohn's disease (CD) being the most common subtypes associated with arthritis and/or spondylitis [22, 85]. Reported prevalence of arthritis in IBD varies depending on disease subtype and joints involved. Some studies have suggested articular manifestations may occur in upward of 39% of patients with IBD [86]. Risk factors for developing IBD-associated arthritis include active bowel inflammation, cigarette smoking, presence of other extraintestinal manifestations, and family history [23, 85–87]. Inflammatory arthritis may present with axial involvement, peripheral involvement, or both. Peripheral and axial joint involvement is similar between UC and CD subtypes with some studies indicating axial disease is slightly more common in patients with CD [24]. Diagnosis of IBD-associated SpA

may require careful attention and a high index of suspicion as presentation may not be clear initially. While most individuals with IBD-associated arthritis have known gut involvement, it is important to recognize inflammatory arthritis can precede the development of clinically apparent IBD. It is also possible for patients with known IBD to experience subclinical musculoskeletal involvement. According to one study, asymptomatic sacroiliitis was detected by radiography in anywhere from 4% to 18% of patients with IBD [88–90]. In general, treatment of IBD-associated arthritis requires addressing both the underlying IBD and joint symptoms. Importantly, studies have shown that treatment of active IBD will improve the associated inflammatory arthritis [24, 91].

10.6.5 Reactive Arthritis

Reactive arthritis is an inflammatory arthritis that develops several days to weeks following exposure to an infectious trigger. Importantly, while associated with infection, it is an aseptic arthritis meaning that no infectious agents can be cultured from the affected joints [92]. Common infectious triggers include *Chlamydia trachomatis*, *Yersinia*, *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia coli*, *Clostridium difficile*, and *Chlamydia pneumoniae*. No preceding infectious agent is identified in up to 40% of patients [92, 93]. Studies of the prevalence and annual incidence of reactive arthritis are highly heterogeneous. However, according to several population-based studies, the annual incidence of reactive arthritis ranges from 0.6 to 27 per 100,000 individuals [93, 94]. Formerly known as Reiter syndrome, reactive arthritis is commonly associated with the clinical triad of postinfectious arthritis, urethritis, and conjunctivitis. These patients represent only about one-third of patients with reactive arthritis [95]. Reactive arthritis typically presents with acute onset of symptoms and should always be considered in young adults presenting with inflammatory arthritis. In addition to the common clinical features of the seronegative SpA, one should inquire about recent infections with particular interest in genitourinary or gastrointestinal symptoms. Additional laboratory evaluation aimed at identifying preceding infectious insults may include stool cultures to test for *Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia*. Urine and genital swab testing can be employed to evaluate *Chlamydia trachomatis* infection using nucleic acid amplification techniques. If detected, treatment of infection is important, particularly with regard to *Chlamydia* as there is demonstrated benefit. Prognosis for reactive arthritis is quite good as more than 50% patients enter permanent remission by 6 months. Of the remaining 50%, up to two-thirds may experience recurrent symptoms, and one-third may go on to develop chronic inflammatory arthritis requiring prolonged immunosuppression [96, 97].

10.6.6 Juvenile Spondyloarthropathy

JSpA is an important type of inflammatory arthritis distinct from other forms of childhood idiopathic inflammatory arthritis. In comparison with the adult forms of SpA, juvenile disease presents with less prominent inflammatory back, reflecting the rare involvement of the sacroiliac and other joints of the spine early in disease. Instead, peripheral arthritis and enthesitis are more common at the time of presentation in JSpA. Due to the lack of inflammatory back pain, it can be difficult to distinguish between JSpA and other forms of chronic inflammatory arthritis in children [98]. According to the International League of Associations for Rheumatology (ILAR) criteria for juvenile inflammatory arthritis, JSpA patients are primarily categorized as enthesitis-related arthritis (ERA), psoriatic arthritis (PsJIA), or undifferentiated arthritis [99]. Other forms of seronegative SpA that may be seen in childhood, such as reactive arthritis and the IBD-associated arthropathies, are not specifically included in the ILAR classification. ERA makes up 10–19% of children classified with JIA. There is a male predominance and mean age of symptom onset is 12 years [100, 101, 102]. The difference between

ERA and PsJIA hinges largely on presence of personal and/or family history of psoriasis but also factors in other items such as presence of nail changes and/or dactylitis. The prevalence of PsJIA is not known with certainty. Treatment of JSpA requires the expertise of a pediatric rheumatologist. As these conditions are chronic in nature, patients will require routine follow-up throughout childhood and adolescence and into adulthood. All attempts to ensure successful transition into adult rheumatology care are critical to long-term health of these individuals.

10.7 Treatment

Management of all of the seronegative SpA subtypes utilizes pharmacologic and nonpharmacologic methods to control symptoms, minimize inflammation, prevent structural damage, and maintain functional capacity. Depending on the subtype of SpA and/or presence of various extra-articular manifestations, patients may require a multidisciplinary approach to care. Dermatologists play an integral role in management of PsA patients as is the case with gastroenterologists in IBD-associated arthritis. In patients with inflammatory eye disease, ophthalmologists are critical for providing information to guide treatment decisions (i.e., determining the presence of active inflammation of the eye).

10.7.1 Nonpharmacologic Strategies

As is the case with any medical condition, patient education is the cornerstone of management. All patients should be educated about the nature of their disease, associated complications, and rationale behind treatment recommendations. Regular discussion should occur with frequent opportunities for patients to ask questions and seek feedback with regard to their knowledge. In general, regular physical activity should be encouraged in all patients. Education regarding joint-protective measures should be provided. Referral to physical and occupational therapy may be warranted in certain cases. While there is no evidence to support any particular diet in treatment of the seronegative SpA, patients should be encouraged to maintain a well-balanced diet. For some patients weight loss may be recommended. Smoking cessation is recommended as tobacco smoking is thought to have a negative impact on seronegative SpA. Finally, yearly influenza immunization is recommended in all patients if not otherwise contraindicated. Other immunizations, including pneumococcal vaccines, may be recommended in certain patients as well.

10.7.2 Pharmacologic Strategies

NSAIDs are the first-line treatment of musculoskeletal manifestations in both axial and peripheral SpAs. According to some reports, they are effective in relieving pain and stiffness in up to 80% of seronegative SpA patients [58, 103]. There is some thought that NSAIDs may also have some disease-modifying properties as well. The choice of NSAID is largely patient dependent (cost, dosing regimen, etc.). Indomethacin is commonly used. All patients should be counseled on the importance of gastric protection while taking NSAIDs. Patients should be advised to take NSAIDs with food or consider the addition of H2 blocker or proton pump inhibitor to prevent NSAID-induced gastritis and peptic ulcer disease. If concern for gastrointestinal risk is high, a COX-2-selective NSAID, such as celecoxib, can be considered. Use of NSAIDs is not appropriate for all patients, particularly those with a history of poorly controlled hypertension, renal disease, cardiovascular disease, and/or prior gastrointestinal ulcer/bleed.

Disease-modifying antirheumatic drugs (DMARDs) may be recommended when disease activity persists despite the treatment with NSAIDs. Conventional, non-biologic DMARDs, like methotrexate (MTX), sulfasalazine (SSZ), and leflunomide (LFN), may be recommended to treat peripheral arthritis but are not as effective in treating axial disease, enthesitis, or dactylitis [104, 105]. In patients with axial disease, enthesitis, dactylitis, and certain extra-articular disease manifestations (inflammatory eye disease, IBD,

psoriasis), treatment with biologic DMARDs is often recommended. The first-line biologic DMARDs are tumor necrosis factor (TNF)-alpha inhibitors including adalimumab, etanercept, certolizumab, golimumab, and infliximab. The choice of anti-TNF-alpha depends on patient factors. For instance, etanercept is not efficacious in the treatment in patients with uveitis and IBD [103, 106]. Other biologic therapies and targeted synthetic DMARDs, like anti-IL-17 and Janus kinase inhibitors, may be recommended based on certain clinical features, the scope of which is beyond this chapter.

Other treatment options like local corticosteroid injections and/or systemic steroids (i.e., prednisone or methylprednisolone) can be considered in some cases. Local corticosteroids can be quite useful in treating localized joint pain, such as a single knee or elbow or even SI joint. Steroid injections can also be useful in treating enthesitis. Oral steroids can be used to treat peripheral joint symptoms in some cases but must be used with caution in PsA as abrupt cessation can cause a significant flare in skin disease [102, 103, 105].

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Systemic Lupus Erythematosus

11

Jacquelyn Smith

Contents

Goals and Objectives

- *Goal*: To provide the reader with an overview on systemic lupus erythematosus (SLE)
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:

1. Epidemiology of SLE
2. Basic pathogenesis of SLE and pathophysiology
3. Organ system involvement that can be seen in lupus
4. Lab serologies seen in SLE and how lupus is diagnosed
5. Some of the different treatments available for SLE

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11.1 Demographics and Epidemiology

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect almost every organ system. It is characterized by a heterogenous presentation, and disease manifestations often evolve over time. It is more common in women, specifically in women of childbearing age (female-to-male ratio 9:1) [1]. In the pediatric populations, the ratio is 2–6:1 and in the elderly 3–8:1, female-to-male (1. SLE Lancet Review). SLE can be seen in all ethnic groups. In the United States, SLE is more common in African-Americans, and African-Americans are more likely to have higher morbidity and mortality than Caucasians [2].

11.2 Pathogenesis and Pathophysiology

The pathogenesis of systemic lupus erythematosus is multifactorial, and depends on numerous factors including genetic predisposition, environmental factors, and alterations in the immune system.

As with most autoimmune diseases, genetics play a role in the development of SLE. There is an 11–50% concordance among monozygotic twins [3], and it is not uncommon to see SLE within families. However, in most patients, these genetics factors need to be triggered by certain environmental factors to become clinically significant. Ultraviolet light is the most implicated environmental factor [4] although there are likely other triggers, including infection.

SLE has been associated with defects in the clearance of apoptotic material.. Increased extracellular debris leads to inappropriate identification of these self-antigens by antigen-presenting cells and the development of autoantibodies. These self-antigens are also identified from neutrophil extracellular traps (NETs); NETs have been correlated with SLE activity. There are also abnormalities identified in T-cell stimulation of B-cells, both because of the types of T-cells that are seen in SLE and the way that they activate B-cells [5]. There are also increased B-cells in patients with SLE which relates to increased antibody production and is a common target in the treatment of SLE [1]. The pro-inflammatory cytokines (such as TNF-alpha, IL-1, IL-6, IFN-gamma, etc.) are also associated with continued inflammation and injury in SLE [1].

11.3 Clinical Manifestations and Disease Course

11.3.1 Constitutional Symptoms

Constitutional symptoms are frequent manifestations of SLE, both at the time of diagnosis and in periods of flare. Fever is a prominent symptom in active lupus, estimated to occur at 41% in one study [6]. Other constitutional symptoms include weight loss and fatigue. About 50% of patients with SLE report severe fatigue, which is comparable to other autoimmune diseases [7]. Fatigue is often profound and functionally limiting. Lymphadenopathy has a prevalence of 5–7% at diagnosis of SLE; typically the cervical and axillary lymph nodes are involved, and lymph node biopsy may be needed in some patients to rule out the possibility of infection or malignancy [8].

11.3.2 Skin and Mucous Membrane Involvement

There are several classic rashes that are associated with SLE, and 72–85% of patients with SLE develop cutaneous manifestations; in about a quarter of patients, it can be the first manifestation of lupus [9]. Acute cutaneous lupus is the classic malar rash, in a butterfly pattern across the nose and cheeks that spares the nasolabial folds. The rash is typically small macules and papules and worsens with sun exposure. Subacute cutaneous lupus is also more commonly seen in UV-exposed areas. The rash can appear as an annular lesion, frequently with scaling, with central clearing. While this rash can cause hypopigmentation, it does not result in scarring. Anti-SSA/Ro and anti-SSB/La are commonly associated with subacute cutaneous lupus [10]. Chronic cutaneous

lupus, conversely, can cause scarring. Discoid lupus is one form of chronic cutaneous lupus. It most commonly affects the face, ears, or scalp, but can become generalized in 20% of cases. Discoid lupus is also more commonly seen in UV-exposed areas.

Alopecia is another cutaneous manifestation of SLE, seen in more than 50% of patients at some point in their disease course [11]. In 30–50% of patients with discoid lesions, the scalp is involved. These lesions can lead to scarring and subsequent hair loss. Patients with SLE can present with diffuse thinning of the hair [11]. Lupus hairs, which are fine hairs along the front of the hairline, are classically found in patients with chronically active SLE and are seen in 5–30% of SLE patients [11].

Oral and nasal ulcers can be reflective of SLE activity. The lesions are often not painful. The oral lesions are found most commonly on the roof of the mouth. Nasal ulcers are likely to be found inside the nares on the septum. Secondary Sjogren's syndrome, characterized by oral and ocular dryness, is reported in 9–33% of SLE patients [12].

11.3.3 Musculoskeletal

Arthritis is seen in 69–95% of SLE patients and can be present in approximately 78% of patients at presentation [13]. Arthritis can be seen in any joint, although small joints are more commonly involved. Erosive arthritis is uncommon in SLE, which differentiates it from rheumatoid arthritis. In general, the arthritis associated with SLE is less inflammatory than rheumatoid arthritis, but redness, warmth, and swelling of the joints can still be seen. Jaccoud's arthropathy is the result of tendon laxity and results in reducible subluxation of the joints that looks very similar to the ulnar deviation or swan neck and boutonniere deformities seen in rheumatoid arthritis. Approximately 3–13% of patients with SLE develop Jaccoud's arthropathy [14].

Avascular necrosis (AVN) can present with new joint pain in SLE patients, especially in the hips or shoulders, although can be seen in many other joints. AVN has been reported at rates of 4–16% in SLE populations [13] and has an association with exposure to corticosteroids. Imaging, either with X-ray or MRI, can confirm the diagnosis. Surgery is often required for treatment. Other musculoskeletal conditions can also occur in patients with SLE.

11.3.4 Cardiovascular

Cardiac manifestations of SLE have been described in the myocardium, heart valves, and coronary arteries.

Pericarditis can be seen in up to 25% of patients with SLE at some point during their disease course, and often presents in conjunction with pleuritis [15]. Pericarditis presents with chest pain that improves with leaning forward, shortness of breath and possibly tachycardia, and diffuse ST segment elevation and PR depression on electrocardiogram. Imaging may reveal a thickened pericardium, often with a pericardial effusion. Large pericardial effusions and even cardiac tamponade can occur in SLE patients and may require emergent pericardiocentesis. Pericardial fluid is exudative with a high neutrophil predominance [15]. Mild cases can be treated with NSAIDs, while more severe cases require steroids with a taper to a steroid-sparing medication.

Involvement of the myocardium is less common. Pathology of lupus myocarditis shows mononuclear cell infiltrates, perivascular inflammation or arteriopathy, and necrosis of the cardiac cells [15], although biopsy is not required for diagnosis. Chest pain and symptoms of heart failure in conjunction with imaging findings consistent with myocarditis (echo or cardiac MRI) can help with diagnosis.

Coronary artery disease is the most common cause of mortality either in patients with longstanding SLE or in those patients with late-onset SLE [15]. Patients with SLE are also more prone to early atherosclerotic disease, likely from a variety of factors. Aside from the standard cardiovascular risk factors (smoking, family history, elevated cholesterol), the persistent

exposure to inflammation from autoimmune disease is likely also playing a role in the development of atherosclerotic disease. Frequent and sometimes prolonged exposure to corticosteroids needed for treatment of SLE manifestations also increases the risk of atherosclerotic disease. Corticosteroids increase blood pressure, serum glucose levels, and body weight, all of which increase the risk of coronary artery disease. Because of this, discussion about lifestyle modification and treatment with antihypertensives and statins when indicated should be a part of the long-term treatment of patients with SLE.

Libman-Sacks endocarditis is a noninfectious endocarditis associated with SLE. Prevalence ranges from 11% to 74%; however, it is not clinically significant in all of these cases [15]. Diagnosis is usually based on echocardiogram findings. Pathophysiology of Libman-Sacks endocarditis is likely immune complex deposition on the heart valves; it can cause valvular insufficiency and some patients need valve replacement or repair.

Children of mothers who have SLE may also have cardiac disease. In pregnant women, anti-SSA/Ro antibody can cross the placenta and cause fetal heart block. In this situation the fetus is monitored closely through gestation; hydroxychloroquine may decrease rates of fetal heart block [16].

11.3.5 Lungs

Symptomatic pleuritis occurs at some point in the disease in 30–50% of patients with SLE, and in 5–10%, it can be the initial manifestation of SLE [17]. Pleuritis presents as chest pain with deep inspiration with pleural effusions. Similar to pericardial fluid, pleural fluid is exudative; another analysis shows a moderately low glucose, low complements, and a positive ANA [17]. If effusions are small, NSAIDs or steroids may be adequate for treatment. Larger or refractory effusions may require percutaneous drainage, higher doses of steroids, or immunosuppressive therapy.

1–12% of patients with lupus develop acute lupus pneumonitis; these patients present with fever, cough, pleuritic chest pain, dyspnea, and hypoxia [17]. The majority of patients are anti-double-stranded DNA positive [17]. Imaging usually reveals alveolar pulmonary infiltrates mostly in the lower lobes and pleural effusions may be present [17]. Previously, the short-term mortality was 50% and worse for patients who develop this while postpartum, but with critical care support, the mortality has improved [17]. Patients are usually treated initially with high-dose corticosteroids and additional immunosuppressive agents.

In patients with long-standing SLE, interstitial lung disease is seen in 3–13% of patients and is associated with an SSA antibody [17]. Patients present with shortness of breath, hypoxia, and restrictive patterns on pulmonary function tests with a decreased diffusion capacity. Imaging reveals ground-glass opacities and fibrosis, typically in the lower lobes. Biopsy is sometimes needed to confirm the diagnosis. Initial treatments are corticosteroids and then immunosuppressive medications if response is favorable.

Shrinking lung syndrome, or vanishing lung, is also seen in SLE, although is not very common. Patients present with shortness of breath and decreased exercise tolerance. Chest imaging shows an elevated hemidiaphragm and decreased lung volumes. Pathophysiology of shrinking lung is not fully understood. Treatment with immunosuppressive agents usually improves symptoms [17].

Diffuse alveolar hemorrhage is a feared complication of SLE and may be fatal. Patients present acutely with dyspnea and hemoptysis. Imaging shows alveolar infiltrates, and diagnosis is typically based on bronchial alveolar lavage (BAL). The classic finding on BAL is serial aliquots of alveolar lavage showing progressively bloody fluid. Patients require high-dose corticosteroids and plasma exchange, followed by immunosuppressive with cyclophosphamide [17].

11.3.6 Nervous System

CNS manifestations of SLE, or neuropsychiatric lupus, range from headaches to seizures, altered

mental status, psychosis, neuropathy, and demyelinating disease.

Headaches are common in patients with SLE, but are not always related to SLE activity. Patients with SLE also commonly describe cognitive impairment that is typically difficult to identify and treat [18].

Psychosis, presenting with delirium or altered mental status, has a prevalence of 1–11% in SLE [19]. It is important to evaluate patients who present with acute mental status changes for infection prior to treatment. If psychosis is attributed to SLE activity, then treatments are glucocorticoids and often other immunosuppressive medications. It is important to remember that steroid medications alone can cause psychosis and personality changes and should be considered in the differential diagnosis of any SLE patient with an altered mental status.

Seizures occur in 8–18% of patients with SLE [19]. This is more likely to occur early in the disease course, usually within the first year [19]. Studies suggest that 3–15% of patients with SLE will have a stroke at some point during their disease [19]. There are several reasons for increased risk of stroke. The accelerated coronary atherosclerotic disease also correlates to increased cerebral atherosclerotic disease. Patients with antiphospholipid antibodies are at increased risk of blood clot, and subsequently stroke. Vasculitis is also seen in SLE patients and may also contribute to risk of stroke.

Transverse myelitis is another devastating neurologic manifestation of SLE, occurring in only 1–2% of patients with SLE but can be the initial presentation in 46% of those patients [19]. Patients present with acute onset of neurologic deficits that can be localized to the spinal cord; brain and spinal cord MRI findings are usually diagnostic. Treatment is with high-dose corticosteroids followed by additional immunosuppressive medication.

11.3.7 Hematologic

SLE can affect all three hematologic cell lines. Anemia affects more than 50% of patients at some point throughout the disease course [20]. There are several etiologies for anemia, although anemia of chronic disease is the most common [20]. Anemia of chronic disease is characterized by irregularities in iron utilization and erythrogenesis that results in a normocytic anemia. Patients with SLE are also at risk of iron deficiency anemia from a number of causes. Autoimmune hemolytic anemia (AIHA) is the development of antibodies to red blood cells. The prevalence of AIHA in SLE is not entirely clear; however, it is included as one of the diagnostic criteria for SLE.

Leukopenia is part of the diagnostic criteria of SLE. Lymphopenia and neutropenia are the most common cell lines affected. One study revealed that at the time of diagnosis, 75% of patients had lymphopenia [20]. Pathogenesis of both can be either antibodies directed against the cells or decreased production due to effects on the bone marrow. Many of the immunosuppressive medications used to treat SLE can also cause leukopenia, so a thorough medication review is necessary in a SLE patient with new cytopenia.

Immune thrombocytopenia is another form of antibody-driven cytopenia seen in SLE, usually treated with steroids in the acute setting.

Patients with SLE have increased likelihood of antiphospholipid antibodies, which increase the risk of thrombosis. The specific factors associated with antiphospholipid are B2-glycoprotein antibody, lupus anticoagulant, and anticardiolipin antibody. The presence of antiphospholipid antibodies increases the risk of pregnancy loss as well. Anticoagulation may be required to prevent fetal loss.

11.3.8 Renal Disease

Renal disease, a major cause of morbidity and mortality in SLE, is present in up to 60% of patients with SLE, with 25–50% having some degree of renal improvement at presentation [21]. Lupus nephritis prevalence varies based on ethnic groups. African-American and Hispanic patients with SLE are more likely to have severe cases of lupus nephritis. Lupus nephritis can be the presenting manifestation of SLE. 10% of patients with lupus nephritis progress to end-stage renal disease [22]. Patients with SLE should be screened regularly for nephritis, and a rise in creatinine, or urine protein or blood, should raise suspicion for

renal involvement. Kidney biopsy is used to diagnose lupus nephritis. Lupus nephritis can have a waxing and waning clinical course and usually develops early in SLE. Patients can present with hypertension and peripheral edema; there is usually an increase in serum creatinine and protein, red blood cells, or red blood cell casts in urine.

There are six classes of lupus nephritis. Classes I and II show variable degrees of mesangial complex deposition and may not need aggressive immunosuppression [23]. Classes III and IV are proliferative lesions and almost always require IV corticosteroids followed by immunosuppression – usually either mycophenolate mofetil or cyclophosphamide although other agents can be used [23]. Most patients with class III and class IV lupus nephritis are treated with induction therapy with a strong immunosuppressant and then with maintenance medication [23]. Class V lupus nephritis is a membranous disease presenting with significant proteinuria that may need medical treatment and management although immunosuppression may not be needed [23]. Class VI is advanced sclerosing lupus nephritis and does not respond to immunosuppression [23].

11.4 Autoimmune Serologies

The antinuclear antibody (ANA) is a screening test for connective tissue disease, including SLE. The ANA test is an immunofluorescence assay against the antibodies which indicates both the pattern and titer (which is reflective of how strongly positive the ANA is in the sample). The ANA is a highly sensitive, nonspecific, test and by itself cannot establish a diagnosis of SLE. The higher the titer, the more likely it is to be related to SLE or another similar disease.

A careful workup will include the evaluation of other autoantibodies that have a higher specificity for SLE. Anti-Smith antibody is seen in about 30% of patients with SLE and is highly specific [24] for SLE. SSA (Ro) and SSB (La) antibodies can also be positive in SLE and may be reflective of secondary Sjogren's syndrome. The presence of a SSA/Ro antibody carries a risk of fetal heart block and neonatal lupus in pregnant patients. Antibodies to double-stranded DNA are relatively specific for SLE, and the titer can correlate with disease activity. Complement consumption will cause the C3 and C4 to drop and may also be a biomarker of SLE activity.

11.5 Diagnosis

The diagnosis of SLE is based on a combination of clinical presentation, pattern of organ involvement, autoantibody profile, and other laboratory testing. The two major classification criteria for SLE are the ACR criteria and the SLICC criteria. These criteria were developed to assure accurate diagnosis for patients entering clinical trials but can be a useful guide in the evaluation of patients with suspected SLE (Tables 11.1 and 11.2).

Table 11.1 ACR criteria (need 4 of 11 criteria)

Malar rash	Renal disorder (proteinuria, casts)
Discoid rash	Neurologic disorder (seizures, psychosis)
Photosensitivity	Hematologic disorder (cytopenia)
Oral ulcers	Immunologic disorder (positive LE cell preparation, anti-DNA, anti-Smith, false-positive syphilis testing)
Arthritis (2+ joints)	Antinuclear antibody
Serositis (pleuritis, pericarditis)	

Tan et al. [25]

Table 11.2 SLICC criteria (need 4 of 17, at least 1 from each category or lupus nephritis on biopsy)

Clinical criteria	Immunologic criteria
Acute cutaneous lupus (malar rash, photosensitivity)	Elevated ANA
Chronic cutaneous lupus (discoid rash)	Elevated anti-dsDNA
Oral ulcers	Anti-smith
Nonscarring alopecia	Antiphospholipid antibody positive
Synovitis in 2+ joints	Low complement
Serositis (pleuritis, pericarditis)	Direct coombs test positive (without hemolytic anemia)
Renal (proteinuria, RBC casts)	
Neurologic (seizures, myelitis, psychosis)	
Hemolytic anemia	
Leukopenia or lymphopenia	
Thrombocytopenia	

Petri et al. [26]

11.6 Treatment

Effective treatment of the patient with SLE requires a careful assessment of the pattern of organ involvement and the disease activity. Therapy will be tailored to the disease manifestations and severity over time. Therapies are targeted at controlling inflammation and preventing organ damage.

11.6.1 Lifestyle Modifications

As previously discussed, UV light exposure is a known trigger in systemic lupus erythematosus, playing a role in both the pathogenesis of disease and also in worsening cutaneous manifestations. Patients with SLE should be counseled to minimize sun exposure and to wear sunscreen, hats, and clothing that covers the skin if they will be in the sun. Smoking cessation is strongly recommended as it is an additional cardiovascular risk factor. Exercise is an important part of a healthy lifestyle, and that includes SLE patients. Exercise can mitigate some of the adverse effects of decreased bone density and weight gain from steroids and the increased cardiovascular disease from inflammation. While photosensitivity, arthritis, and specific organ involvement may limit certain activities, it is important to encourage patients with SLE to exercise as their disease activity permits. Studies have shown that exercise can improve fatigue and depression as well [27].

11.6.2 Pharmacologic Therapy

11.6.2.1 Hydroxychloroquine

Hydroxychloroquine (HCQ), an immunomodulatory agent, is the cornerstone of SLE treatment. HCQ is particularly effective in managing the skin and joint manifestations of SLE. It has a slow onset of action and it may take up to 3 or 4 months to see a clinical benefit. It is safe in pregnancy and should be continued throughout pregnancy and during lactation. HCQ is not immunosuppressive so it does not increase the risk of infection. Hydroxychloroquine has been shown to improve survival and decrease disease flares in SLE. It has mild anticoagulant effects and may decrease the risk of blood clots [28]. Over years of use, cumulative plaquenil use can cause retinal toxicity, so all patients should undergo eye examination annually [29].

11.6.2.2 Corticosteroids

Corticosteroids can effectively and rapidly control inflammation in SLE. Steroids are used in the setting of impending organ failure, as high doses can be given to act quickly to control inflammation and prevent further organ damage. Long-term use should be minimized due to significant risks of osteoporosis, weight gain, diabetes, neuropsychiatric effects, infections, and others [30]. High doses, or pulse doses, of steroids are reserved for severe organ involvement (such as lupus nephritis or CNS involvement). Moderate doses are used for less severe organ involvement or serositis. Low doses of steroids can be used to treat cutaneous or musculoskeletal symptoms. All efforts should be made to minimize the steroid dose to prevent side effects.

11.6.2.3 Immunosuppressants

Cyclophosphamide is a chemotherapeutic agent that is reserved for severe organ involvement, such as lupus nephritis or neuropsychiatric lupus. Mycophenolate mofetil is also used in lupus nephritis. Azathioprine is one of the few medications that can be used during pregnancy – it can be used for myositis, lupus nephritis in remission, and skin disease. Methotrexate is a good agent for inflammatory arthritis, but can also be used in skin disease or muscle inflammation. All of these medications, by process of lowering the immune system, carry an increased risk of infection and require careful monitoring for toxicity.

11.6.2.4 Biologic Therapy

Belimumab is a human monoclonal antibody that inhibits BLyS, which is a B-cell-activating factor and is available as an infusion or a subcutaneous injection [31]. Belimumab is FDA approved for the treatment of active autoantibody-positive SLE that has not responded to standard therapy. It is not indicated for the treatment of lupus nephritis.

IVIG or plasma exchange can also be used in critical illness. Rituximab, a monoclonal antibody against B-cell receptor CD20, has not been shown to be useful in lupus nephritis but can be used for other manifestations of SLE such as arthritis, myositis, and serositis.

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Crystalline Arthropathy

12

Rami ElTaraboulsi

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the diagnosis and management of crystalline arthropathy, specifically gout and calcium pyrophosphate deposition disease.
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe the:

1. Epidemiology of gout and calcium pyrophosphate deposition disease
2. Pathophysiology of gout and calcium pyrophosphate deposition disease
3. Clinical presentations of gout and calcium pyrophosphate deposition disease
4. Role of synovial fluid analysis and imaging in the diagnosis of gout and calcium pyrophosphate deposition disease
5. Treatment strategies for both acute and chronic subtypes of gout and calcium pyrophosphate deposition disease

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12.1 Gout

Gout is an inflammatory arthritis caused by deposition of monosodium urate crystals in the joints and surrounding soft tissue. It is typically characterized by acute attacks but can also exist in a chronic form. Gout management focuses on decreasing acute inflammation and lowering the serum uric acid level to prevent future attacks and resultant joint damage.

12.1.1 Epidemiology

The prevalence of gout is estimated to be 3.9% among US adults with men more commonly affected than women, although the incidence rate tends to even out after the menopause. The incidence increases with age and is more common after the fourth decade of life. The mean serum urate levels also appear to be higher for men with gout compared to women [1]. There are several risk factors associated with gout including age, diabetes mellitus, obesity, hypertension, and chronic kidney disease [2]. Dietary factors such as consumption of foods high in purines and alcohol also contribute to hyperuricemia. When gout occurs in young patients, it is almost universally associated with an inborn error of metabolism leading to overproduction of uric acid.

12.1.2 Pathophysiology

Hyperuricemia (typically >6 mg/dl) is the major contributing factor in the development of gout. It may occur due to either overproduction of urate or underexcretion due to renal disease. Although all patients who ultimately develop gout will have a history of hyperuricemia, the presence of hyperuricemia alone does not assure the development of gout. The higher the level of serum uric acid, the greater the risk for incident or recurrent gout [3]. The progression to clinical gout is complex with many factors such as genetics, co-morbidities, and environment playing a role [4]. Recent studies have demonstrated the importance of the gene ABCG2 in the onset of gout and progression of disease [5]. Acute gout may be triggered by trauma, surgery, excess alcohol, aggressive diuresis, or drugs that alter urate levels (e.g., low-dose aspirin, cyclosporine). This leads to de novo formation of monosodium urate crystals or release of microcrystals already present in the joint. Acute gout is characterized by an inflammatory response with synovial hyperplasia and infiltration by neutrophils, mononuclear phagocytes, and lymphocytes. Particularly it is the phagocytosis of MSU crystals by neutrophils that causes an inflammatory cascade with the activation of the NLRP3 inflammasome. The NLRP3 inflammasome then causes proteolytic cleavage of IL-1 beta leading to IL-1 receptor activation. The IL-1 pathway is responsible for releasing secondary inflammatory mediators such as prostaglandins, cytokines, and chemokines. The IL-1 pathway has been implicated in many autoinflammatory conditions and is a potential target for treatment [6].

12.1.3 Clinical Presentation

The initial presentation of gout consists of an acute and severe onset of redness, swelling, and warmth, usually of a single joint (acute monoarthritis). Symptoms usually reach maximum intensity in the first 24 hours. Attacks will generally resolve within days to weeks even without treatment. The first attack of gout classically involves the first metatarsophalangeal joint (also known as podagra) but gout can occur in any joint. Recurrent attacks can involve other joints such as a knee, ankle, wrist, elbow, or hand. Rarely, gout can attack the spine and sacroiliac joints [7]. Occasionally, gout will affect multiple joints at once and this is called polyarticular gout. Polyarticular gout is typically seen in patients with longstanding disease. The joint involvement can be simultaneous or occur in a migratory fashion. It can also present with fevers and mimic sepsis [8].

Chronic gout is characterized by the deposition of tophi or collections of MSU crystals within the joint and soft tissues. The term tophaceous gout describes severe and often disabling

disease with destructive changes within the joint. The erosive joint damage can sometimes mimic osteomyelitis or other forms of inflammatory and erosive arthritis such as RA and may lead to incorrect treatment. Tophi are usually apparent on physical exam and can be seen on the ears or in the soft tissues surrounding joints or in bursa, such as the olecranon bursa. Tophi may ulcerate and a chalky, white substance can be expressed. When examined under polarized microscopy, monosodium urate crystals will be demonstrated. Patients with tophaceous gout typically have a large urate burden and may have refractory disease.

12.1.4 Diagnosis

The gold standard for the diagnosis of gout is arthrocentesis and synovial fluid analysis. The synovial fluid should be inflammatory with >5000 wbc/mm3, but cell counts are often much higher. Identification of *intracellular* MSU crystals that are needle-shaped and negatively birefringent on polarized light microscopy confirms the diagnosis. If arthrocentesis cannot be performed, gout may be diagnosed based on history, physical exam, laboratory studies, and imaging. The ACR/EULAR gout classification criteria (see Table 12.1) can be a helpful tool in which providers can input patient characteristics to determine the likelihood of gout [9]. Of note, serum uric acid levels may be normal or low during attacks, and therefore a level obtained after resolution of the acute attack may be more helpful. Plain radiographs may show the classic gouty erosions with overhanging edges (see Figs. 12.1 and 12.2) but this is a late finding. Ultrasound is a valuable tool for the detection of monosodium urate deposition in cartilage. The "double contour sign" is a hypoechoic band located over the superficial margin of the cartilage and has shown good sensitivity (60%) and excellent specificity (91%) when compared to the gold standard of MSU crystal identification on synovial fluid analysis [10]. In addition, dual-energy CT is becoming increasingly used in the diagnosis of gout. The differential diagnosis of an acute

Table 12.1 The 2015 ACR/EULAR gout classification criteria. Gout diagnosis requires identification of MSU crystals in a symptomatic joint or acquiring ≥8 points in the above domains [9]

Domain	Point assignment
Pattern of joint involvement	Ankle or mid-foot (1) Podagra (2)
Characteristics Erythema overlying joint Cannot bear touch or pressure Difficulty walking/using the joint	One characteristic (1) Two characteristics (2) Three characteristics (3)
Time course of typical episode (≥2 following met) Maximal pain within 24 hours Resolution of symptoms within 14 days Complete resolution between attacks	One typical episode (1) Recurrent typical episodes (2)
Clinical evidence of a tophus	Present (4)
Serum uric acid level	<4 mg/dl (−4) 6–8 mg/dl (2) 8–<10 mg/dl (3) ≥10 mg/dl (4)
Synovial fluid analysis of a symptomatic joint	MSU negative (−2)
Imaging Ultrasound detection of urate deposition DECT demonstrating urate deposition	Either present (4)
Imaging X-ray showing typical gout erosion	Present (4)

Fig. 12.1 There is a large tophus surrounding the first MTP joint (arrow), which is a typical location for gouty arthritis. There is also evidence of bony erosion

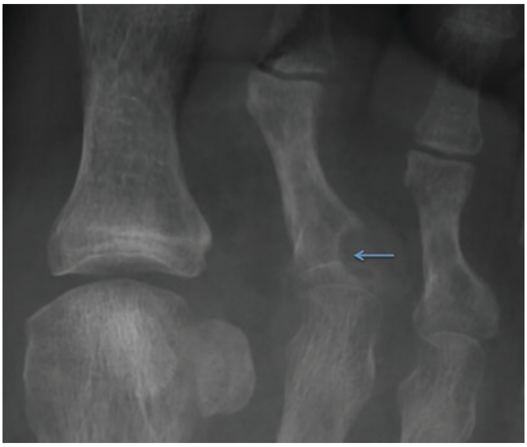

Fig. 12.2 There is an overhanging erosion (arrow) at the base of the second proximal phalanx of the foot

inflammatory arthritis also includes septic arthritis, pseudogout (CPPD), rheumatoid arthritis, and trauma. A synovial fluid analysis is essential when there is a high index of suspicion for infection.

12.1.5 Treatment

12.1.5.1 Lifestyle Modifications

Patients should be counseled on lifestyle factors that increase their risk for gout attacks. Purine intake, particularly from red meat and seafood, should be limited [11]. Limiting alcohol intake especially for heavy drinkers is also beneficial. For patients who are obese, weight loss can reduce serum uric acid levels and is strongly recommended [12]. For patients who have hypertension and gout, avoidance of thiazides and loop diuretics are recommended since these can increase urate levels. If an antihypertensive is needed, an ARB or ACE inhibitor may be helpful since they have mild uricosuric effects [7, 13].

12.1.5.2 Pharmacologic Therapy

The treatment of gout depends on the number of joints involved, the chronicity of disease, and co-existing medical conditions (particularly kidney disease, renal transplant). Treatment of acute gout includes the early use of non-steroidal anti-inflammatories (NSAIDs) and/or colchicine to treat the active inflammation. Intraarticular steroids may be given for those with only one or two joints affected. For severe polyarticular flares, oral steroids are generally required starting at moderate to high doses. Oral steroids should also be considered in patients with contraindications to NSAIDs or colchicine.

Recurrent attacks of gout (at least two per year), tophi, and history of nephrolithiasis are all indications for urate-lowering therapy. The therapeutic goal is to reduce the uric acid below a certain threshold (typically <6 or <5) to prevent further gout attacks and joint damage [7]. Medications can decrease urate production (xanthine oxidase inhibitors such as allopurinol or febuxostat), convert urate to soluble form (pegloticase), or excrete urate through the renal system (uricosurics such as probenecid, lesinurad). Allopurinol is generally considered first line due to good efficacy and affordability. Patients are at risk of gout attacks when initiating urate-lowering therapy and therefore concomitant use of prophylaxis with colchicine or NSAIDs is recommended until the target serum urate concentration (<6 mg/dL) is reached.

Patients with advanced kidney disease can present a therapeutic challenge. Uricosuric agents are contraindicated in patients with GFR < 30. Allopurinol can be safely used in patients with renal impairment, starting at a low dose (50 mg) and titrating up slowly and monitoring for toxicity [14]. Colchicine requires a dose reduction and toxicity and careful monitoring. Patients on allopurinol should be counseled regarding potential for a drug hypersensitivity reaction and potential for drug-drug interaction. Colchicine can cause myopathy and neuromyopathy and interact with other medications [7, 15].

12.2 Calcium Pyrophosphate Dihydrate Deposition (CPPD) Arthropathy or Pseudogout

Calcium pyrophosphate dihydrate deposition (CPPD) disease is a broad term describing the types of conditions that occur from calcium pyrophosphate deposition within joints and soft tis-

sue. Similar to gout, it can occur in an acute/episodic form ("pseudogout"), chronic form, or an asymptomatic form (chondrocalcinosis).

12.2.1 Epidemiology

CPPD arthropathy has been estimated to affect about 7% of the US population and has a strong association with older age with most patients above the age of 50. There does not seem to be a gender predominance. Osteoarthritis is commonly seen with CPPD and is a recognized risk factor. Secondary causes and other risk factors for CPPD disease include hyperparathyroidism, hemochromatosis, hypomagnesemia, hypophosphatasia, and severe chronic kidney disease [16].

12.2.2 Pathophysiology

The pathogenesis of crystal formation in CPPD disease is poorly understood. There is overproduction of pyrophosphate in the cartilage which leads to supersaturation and crystal deposition. Similar to gout, the crystal deposition will trigger an inflammatory response with infiltration of neutrophils into the joint space. The crystals activate synovial fibroblasts and chondrocytes. Inflammasome activation and release of IL-1B is thought to be a key step in the pathogenesis of CPPD disease [17]. There is a predilection for joints with prior evidence of osteoarthritis highlighting the prerequisite of altered synovium [18].

12.2.3 Clinical Presentation

There is a subgroup of patients with CPPD who are asymptomatic and will only have demonstration of chondrocalcinosis on plain radiographs. These patients often have osteoarthritis which can make it difficult to determine the etiology of their pain. Generally, osteoarthritis will follow an insidious course, whereas CPPD disease will have an identifiable onset. In the acute form of CPPD disease, there is an abrupt onset of painful joint swelling that typically reaches maximum intensity in less than 24 hours. It can occur as a monoarthritis or oligoarthritis. Constitutional symptoms such as fevers and chills are not uncommon and can accompany the joint pain. The typical joints affected include the knee, wrist, elbow, and shoulder. The first MTP is not commonly affected and can help differentiate CPPD from gout. The attacks generally last longer than gout and can take weeks to subside. Acute attacks can be triggered by multiple situations including surgery, trauma, or acute illness. The surgeries that most commonly cause flares include parathyroidectomy and hip fracture repair [19]. Medications such as loop diuretics and bisphosphonates can trigger flares.

CPPD arthropathy may have a number of unique clinical phenotypes. The most common is CPPD associated with osteoarthritis which is often polyarticular. It affects joints commonly seen in osteoarthritis including hips, knees, and interphalangeal joints but should be suspected in someone with osteoarthritis in atypical areas such as MCPs, wrists, elbows, and shoulders. It can have similar findings to osteoarthritis on exam with bony enlargement, crepitus, joint swelling, and restricted range of motion. Another form of CPPD arthropathy can present like rheumatoid arthritis. This pseudo-RA form is characterized by an inflammatory arthritis affecting the small joints in a symmetric pattern which may be clinically indistinguishable from RA. Laboratory evaluation and imaging will help lead to a correct diagnosis [19, 20]. Other rare phenotypes of CPPD include spinal involvement, most often involving the C-spine and a destructive arthritis resembling a neuropathic arthropathy. Crowned dens syndrome is a rare syndrome seen with CPPD disease affecting the C2 vertebra and can often present with a clinical picture resembling meningitis due to fevers, severe neck pain, and elevated inflammatory markers [19].

12.2.4 Diagnosis

The hallmark of CPPD disease is the presence of calcium pyrophosphate crystals on polarized light

microscopy on synovial fluid analysis. These crystals are usually rhomboid shaped but are often pleomorphic and weakly positively birefringent. In acute CPPD arthropathy, as in other inflammatory conditions, the synovial fluids will have a high leukocyte count (often above 10,000 per mm^3). The synovial fluid in chronic CPPD disease will have a lower cell count and may be normal. In acute CPPD arthropathy the crystals will be intracellular. Extra-cellular CPPD crystals may be seen on synovial fluid analysis in CPPD arthropathy but may also be seen in the setting of osteoarthritis and may not have any clinical significance. When the synovial fluid is inflammatory, septic arthritis should always be ruled out with gram stain and culture since this can cause a similar presentation. Patients can have co-existing gout with CPPD disease; therefore, synovial fluid is often needed for diagnosis. In patients who are young or present atypically, then one should consider secondary CPPD in which case a metabolic workup should be performed checking renal function, electrolytes, parathyroid hormone, thyroid studies, and iron panel.

Diagnostic imaging can also be helpful in diagnosing a patient with CPPD disease. Plain films of the affected joint often show chondrocalcinosis (see Fig. 12.3). If there is still a high suspicion for CPPD but no chondrocalcinosis is seen in the symptomatic joint, then one can look for other commonly affected joints such as the knee, wrist, or pelvis [20]. Other radiographic findings that can be seen in CPPD disease include hook-like osteophytes of the MCPs, articular destruction, joint space narrowing, subchondral cyst formation, subchondral collapse, and spinal involvement. There can also be calcifications of tendons including the Achilles, quadriceps, and rotator cuff [19].

Figure 12.4 shows a patient with CPPD disease with a hook-like osteophyte of his MCP joint (arrow) as well as joint space narrowing.

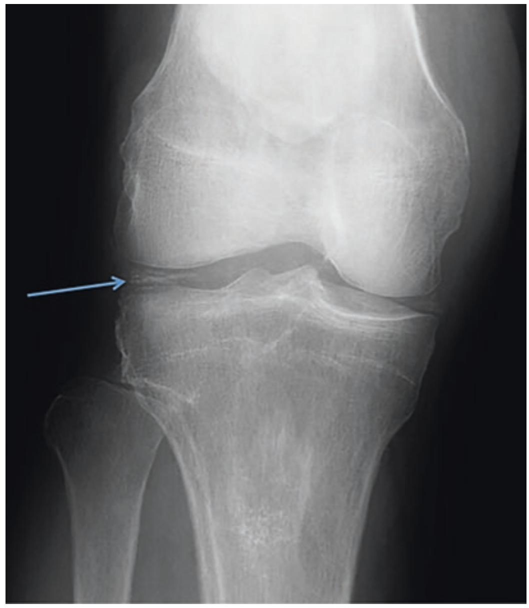

Fig. 12.3 Chondrocalcinosis or deposition of calcium is seen in the femorotibial joint in this patient with CPPD disease

Fig. 12.4 This patient with CPPD disease has a hook-like osteophyte of his MCP joint (arrow) as well as joint space narrowing

12.2.5 Treatment

The goals of treatment of acute CPPD focus on reducing pain and joint inflammation. Patients with one or two joints involved may be candidates for arthrocentesis and corticosteroid injection. If there is concern for septic arthritis, then injection

should be deferred until infection has been ruled out. For patients with several joints involved, early use of non-steroidal anti-inflammatories can be beneficial, but the benefits should be weighed against the risks in this population. In patients who have contraindication to NSAIDs, colchicine can be used and has shown similar efficacy. For those who cannot tolerate or have not improved with first-line treatments, then oral corticosteroids can be used in low to moderate doses. Patients who require corticosteroids will often need slow tapers in order to avoid recurrent flares. In patients who have three or more attacks per year, colchicine can be used daily as prophylaxis.

For those with chronic CPPD arthropathy, treatment options are limited. NSAIDs should be used as initial treatment but there is increased toxicity with long-term use. Second-line treatments include colchicine, hydroxychloroquine, and low-dose oral corticosteroids. Recent data shows that those with resistant disease may benefit from a disease-modifying agent such as methotrexate [21], but data are mixed. Those with co-existing osteoarthritis may benefit from pain management strategies, reserving joint replacement as last resort.

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Part III

Musculoskeletal Infection, Vascular, and Neoplastic Diseases

13 Microbes in Bone and Joint Infections

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Contents

Goals and Objectives

- *Goal*: To introduce the reader to the diagnosis and management of bone and joint infections.
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Common causes of bone and joint infections
  2. Diagnosis of bone and joint infections, including the use of appropriate imaging modalities
  3. Therapy of common bone and joint infections

13.1 Osteomyelitis

13.1.1 Introduction

Osteomyelitis is the infection of bones. It is acquired either hematogenously (i.e., in the setting of bacteremia from another source), through direct inoculation (i.e., osteomyelitis after open fracture or post-surgical osteomyelitis), or through a contiguous source (i.e., osteomyelitis

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in the setting of an infected diabetic foot ulcer or decubitus ulcer). Acute osteomyelitis is the infection that was acquired recently (~2 weeks of symptoms), while chronic osteomyelitis is the infection that has been going for several (>3) months [1]. Whether the osteomyelitis is acute or chronic can have implications in terms of treatment: acute osteomyelitis can often be treated with antibiotics alone, while in chronic osteomyelitis there is usually bone necrosis, with formation of sequestrum, and surgical debridement is needed in addition to antibiotics. Vertebral osteomyelitis can be also usually cured with antibiotics without the need of debridement.

Pathogens causing osteomyelitis include gram-positive bacteria (such as *Staphylococcus aureus*, coagulase-negative staphylococci, and *Streptococcus* species) and gram-negative bacteria (Table 13.1). In hematogenous osteomyelitis there is often a single pathogen involved, but osteomyelitis in the setting of a contiguous wound or contiguous soft tissue infection (e.g., diabetic foot ulcer-related osteomyelitis or sacral osteomyelitis in the setting of a sacral decubitus ulcer) is usually polymicrobial including gram positives/gram negatives and anaerobes. Occasionally, less frequent organisms can cause osteomyelitis such as fungi or mycobacteria. Also, some pathogens are associated with certain underlying conditions, for example, *Salmonella* with osteomyelitis in patients with sickle cell disease or *Brucella* in the setting of consumption of unpasteurized milk.

The diagnosis of osteomyelitis can sometimes be made clinically, but usually imaging studies are needed (Table 13.2). X-rays should generally be done first. They may show abnormalities such as bone lucencies, but they are not very sensitive, particularly early on, and do not show many details. The best imaging study for diagnosis is MRI which is both very sensitive and specific. Nuclear imaging studies are very sensitive as well and are an alternative diagnostic modality in patients who cannot have an MRI, although they are not as specific and do not show anatomic details. Finally, CT scans and sometimes ultrasounds can be useful in certain cases. In terms of laboratory tests, the inflammatory markers CRP and ESR are typically elevated and can be also followed to assess response to treatment.

To make a microbiological diagnosis, a bone culture is usually needed. This can be obtained through surgical bone debridement or through imaging-guided bone biopsy, and it should be generally done before antibiotics are started to improve microbiologic yield. The bone should be also sent for pathology, which together with culture can confirm the diagnosis of osteomyelitis. Occasionally patients who present with sepsis in the setting of osteomyelitis have positive blood cultures and the pathogen isolated can often be assumed to be the cause of the osteomyelitis. Particularly, in acute hematogenous osteomyelitis

Table 13.1 Pathogens in osteomyelitis

Common
Staphylococcus aureus
Coagulase-negative staphylococci
Streptococcus spp.
Aerobic gram-negative bacilli (Pseudomonas, E. coli, etc.*)*
Enterococcus spp.
Less common
Mycobacterium tuberculosis
Brucella
Salmonella

Table 13.2 Imaging modalities for the diagnosis of osteomyelitis

Imaging	Sensitivity	Specificity	Comments
X-ray	Low	Low	Negative in early osteomyelitis
MRI	High	High	Preferred imaging study. Expensive. Sometimes not an option due to contraindications
CT scan	Mod-high	High	Cannot detect early osteomyelitis. Detailed evaluation of surrounding soft tissues
Nuclear imaging	High	Mod-high	Do not provide anatomic details. Depending on the nuclear imaging study, specificity can be low

Table 13.3 Examples of antibiotics for osteomyelitis

Condition	**Empiric antibiotics**
Diabetic foot ulcer osteomyelitis/sacral decubitus osteomyelitis	Piperacillin/tazobactam ± vancomycin, cefepime + metronidazole ± vancomycin
Vertebral discitis-osteomyelitis	Vancomycin + cefepime
Organism	**Antibiotic regimen**
Methicillin-sensitive *Staphylococcus aureus*	Oxacillin, cefazolin
Methicillin-resistant *Staphylococcus aureus*	Vancomycin, daptomycin
Streptococcus spp.	Penicillin, ceftriaxone
Pseudomonas aeruginosa	Cefepime, ceftazidime, meropenem, ciprofloxacin
Enterobacteriaceae	Ceftriaxone, ciprofloxacin

as well as in vertebral osteomyelitis, blood cultures are frequently positive.

The treatment for osteomyelitis (Table 13.3) often involves long courses of antibiotics (4–6 weeks), which are often given intravenously, although depending on the pathogen, oral antibiotics with good bioavailability and concentration in the bones can be an option. Also, if the infected bone is surgically resected, a brief course of (often oral) antibiotics targeting the surrounding soft tissue infection is often sufficient. In clinically stable patients, especially in the setting of chronic osteomyelitis, antibiotics can be withheld until cultures are taken and a microbiological diagnosis is made. In patients presenting with sepsis, antibiotics are started empirically based on the usual pathogens involved and then narrowed based on cultures. If there is osteomyelitis in the presence of hardware (e.g., osteomyelitis after bone fixation for a fracture), eradication of the infection can be hard and these patients often need chronic suppression with antibiotics [1].

13.1.2 Acute Osteomyelitis

Acute hematogenous osteomyelitis is typically seen in children, usually involving the long bones. *Staphylococcus aureus* is the most common pathogen. Other pathogens include *Streptococcus* spp., such as *Streptococcus pneumoniae*. It typically presents with acute pain and swelling of the involved area as well as fever. X-rays are often negative, while MRIs are diagnostic. Blood cultures are often positive, in which cases there is generally no need for bone biopsy [2]. Treatment consists of antibiotics which are often oral. Duration of treatment for acute osteomyelitis in children is typically 3 weeks.

13.1.2.1 Acute Osteomyelitis in Sickle Cell Patients

Patients with sickle cell disease are at higher risk for acute osteomyelitis. Typical pathogens are *Staphylococcus aureus* and *Salmonella* species. The diagnosis is easy to miss as the pain is often attributed to a sickle cell crisis.

13.1.3 Vertebral Osteomyelitis

Vertebral osteomyelitis usually occurs through hematogenous spread. Sometimes another infection is the cause for the bacteremia, such as endocarditis, but frequently no additional infection is identified and it is thought that the osteomyelitis occurred in the setting of transient bacteremia. Occasionally it can also occur in the setting of a contiguous infection or a vertebral surgery or procedure, such as steroid injection. Typically due to the anatomy of the vascular supply of the vertebrae, the infection involves an intervertebral disc and extends to the two neighboring vertebral bodies [3]. Further extension of the infections can result in development of paravertebral abscesses, such as psoas muscle abscesses, as well as epidural abscesses. Sometimes the infection is located at the facet joints, resulting in pyogenic facet joint infection. In terms of clinical symptoms the patients often have back pain in the involved area, which can often be present for a few months before the diagnosis is made. Fever can be present as well, but a lot of patients are afebrile. In the case of pyogenic facet joint infection, the pain is located more laterally rather than in the midline. If there is development of an epidural abscess, acute onset of neurological symptoms such as paraplegia can occur. On physical exam, there can be focal tenderness over the

involved vertebral bodies. The diagnosis is usually made by an MRI. Blood cultures are often positive. If blood cultures are negative, the microbiological diagnosis can be established by imaging-guided biopsy. In clinically stable patients (no sepsis and no neurological deficits), antibiotics can be held until diagnosis is made. Usually, vertebral osteomyelitis is caused by a single pathogen although polymicrobial infections can occur as well. Typical pathogens are gram-positive bacteria, such as *Staphylococcus aureus*, *Streptococcus* spp., and aerobic gram-negative rods. In the setting of appropriate exposures (consumption of unpasteurized milk and cheese), *Brucella* can be a consideration as well. Medical treatment with antibiotics for 6–8 weeks is usually curative. Surgery may be needed in the setting of an epidural abscess or if no response to medical treatment.

13.1.3.1 Tuberculous Osteomyelitis

Tuberculous osteomyelitis can involve any bones, but more commonly it affects the spine (Pott's disease). Symptoms include back pain and fever and are usually subacute. There can be associated deformity of the infected vertebral body (gibbous) or neurological symptoms from spinal cord compression. On imaging studies the intervertebral disk is often not involved, unlike the usual cases of vertebral osteomyelitis. Diagnosis often requires vertebral biopsy. Medical treatment is often adequate.

13.1.4 Diabetic Foot Osteomyelitis

Diabetic foot osteomyelitis usually occurs in the setting of a neuropathic diabetic foot ulcer. It may be asymptomatic, especially if significant peripheral neuropathy is present, or there can be presence of pain. In the setting of an acute exacerbation, there can be fever and symptoms of surrounding soft tissue infection as well as purulent drainage from the ulcer. Diagnosis can be made clinically if there is probing of the ulcer to bone, but often imaging studies are also needed, such as X-rays and MRIs or CT scans. Infections are often polymicrobial (gram positives, gram negatives, anaerobes), so establishing a microbiological diagnosis by bone biopsy (imaging guided or obtained intraoperatively) is very important to tailor antibiotics. Bone should be also sent for pathology, as particularly in the setting of Charcot foot, it can be very hard to tell if the imaging abnormalities are due to the Charcot foot itself or due to an infection. As with other cases of chronic osteomyelitis, antibiotics can often be held until the diagnostic workup is completed. Combined medical and surgical management is usually needed for the treatment of diabetic foot osteomyelitis. The duration of antibiotics is often for several weeks, but if the infected bone is removed completely surgically, then antibiotics can be discontinued a few days later, once the associated soft tissue resolves and the wound is healing appropriately [4].

13.2 Infective Arthritis

13.2.1 Introduction

Infective arthritis is the infection of native or prosthetic joints. Native joint infective arthritis is typically caused by bacteria or viruses although other pathogens can be involved sometimes. Acute bacterial (septic) arthritis generally involves one joint (mono-arthritis), although oligo-arthritis can be seen in some cases. It is a medical emergency due to the fact that it can result in significant joint damage very rapidly. Typical organisms are *Staphylococcus aureus* and *Streptococcus* spp. In sexually active persons, *Neisseria gonorrhoeae* can be a cause as well (Table 13.4). Some viruses have a propensity for joints, and as a result, patients can present with arthralgias or true arthritis. Usually in those cases a number of joints are involved (oligo-

Table 13.4 Common causes of septic arthritis

Bacteria
Staphylococcus aureus
Streptococcus spp.
Coagulase-negative staphylococci
Gram-negative bacilli
Neisseria gonorrhoeae

arthritis or poly-arthritis). Prosthetic joint infections are typically caused by bacteria and affect about 1–2% of prosthetic joints. They can occur in the first few months after a joint replacement as a result of wound contamination, in which case they are typically caused by skin bacterial such as *Staphylococcus aureus* (usually early onset, i.e., <3 months post-surgery) and less virulent bacteria such as coagulase-negative staphylococci or *Cutibacterium acnes* (delayed onset, i.e., 3–12 months post-surgery). Late infections are often due to hematogenous seeding (typically with *Staphylococcus aureus*).

Patients with infectious arthritis have pain and decreased range of motion of the joint(s) involved as well as erythema and swelling if the joint is superficial. Fever is frequently present as well. Analysis of the synovial fluid is central to the diagnosis of infective arthritis. Aspiration can be done at the bedside for superficial joints such as the knee or under imaging guidance for deeper joints. Synovial fluid should be sent for cell count, crystals, gram stain, and culture. Additional testing may be needed depending on the suspected pathogen. Differential diagnosis includes inflammatory arthritis such as gout and pseudogout and arthritis associated with autoimmune diseases.

Treatment of septic arthritis generally involves drainage of the joint plus antibiotics for several weeks. In cases of prosthetic joint infections, the highest success rates are seen with a two-step joint revision plus antibiotics, but in some cases one-step revision or surgical debridement with liner exchange and retention of the prosthesis may be an option. Viral arthritis management is supportive.

13.2.2 Native Joint Arthritis

13.2.2.1 Bacterial (Septic) Arthritis

Septic arthritis is more common in patients with underlying joint problems, such as rheumatoid arthritis, although it can occur in previously healthy joints as well [5]. The joints of the lower extremities are more commonly involved. It typically involves one joint, although in the setting of underlying joint disease, such as rheumatoid arthritis, more than one joint can be involved. Septic arthritis is most commonly caused by *Staphylococcus aureus* followed by *Streptococcus* spp., but other bacteria can be involved as well (Table 13.4). In sexually active patients *Neisseria gonorrhoeae* can be a cause. Septic arthritis is usually acquired through hematogenous spread in the setting of transient bacteremia or presence of another infection, such as endocarditis.

Patients generally present with acute monoarthritis and fever. The involved joint has significant swelling and erythema, and the range of motion is typically severely diminished. Symptoms and signs can be more indolent in immunosuppressed patients. *Neisseria gonorrhoeae* can cause isolated monoarthritis or, in the setting of disseminated gonococcal infection, can present with a combination of migratory arthralgias, tenosynovitis, pustular rash, and oligoarthritis.

Septic arthritis generally results in significant inflammation of the synovial fluid (>50,000 WBC/uL). Gram stain can be positive in ~50% of patients and culture is usually positive. Blood cultures can be positive in the setting of bacterial arthritis and should be sent as well. For gonorrhea, synovial fluid cultures are often negative and the diagnosis is often made by detection of *Neisseria gonorrhoeae* in the genital tract (by *Neisseria gonorrhoeae* NAA).

Treatment consists of antibiotics (Table 13.5) and drainage of the joint. Drainage can be done by daily aspiration of the joint or by surgical

Table 13.5 Examples of antibiotic regimens for septic arthritis

Organism	Antibiotics
Methicillin-sensitive *Staphylococcus aureus*	Oxacillin or cefazolin × 4 weeks
Methicillin-resistant *Staphylococcus aureus*	Vancomycin × 4 weeks
Streptococcus spp.	Penicillin G or ceftriaxone × 4 weeks
Enterobacteriaceae	Based on sensitivities
Neisseria gonorrhoeae	Ceftriaxone × 1–2 weeks
Borrelia burgdorferi (Lyme)	Doxycycline × 4–8 weeks

wash-out. Duration of antibiotics is about 4 weeks for uncomplicated cases, either intravenously for the whole duration of treatment or IV antibiotics can be changed to oral antibiotics (if oral antibiotics with good bioavailability are available) after the first 2 weeks. For gonococcal arthritis antibiotics alone for 1–2 weeks are usually sufficient.

Lyme Arthritis

Lyme arthritis can be a late manifestation of infection with *Borrelia burgdorferi*, usually presenting several months from the initial infection. It usually presents as monoarthritis or oligoarthritis [6]. The knee joints are typically involved. Patients often present with joint swelling and pain without other symptoms. The patients often do not recall a tick bite and frequently have not had any other symptoms of Lyme disease previously. Synovial fluid is inflammatory with a WBC that ranges usually between 10,000 and 20,000 WBC/uL. Lyme Western blot in the serum is strongly positive in most cases, and a negative Lyme serology makes the diagnosis of Lyme arthritis very unlikely. Positive Lyme PCR in the synovial fluid can confirm the diagnosis but it is not very sensitive. Treatment consists of oral doxycycline for 4–8 weeks. In patients who do not respond to doxycycline, IV ceftriaxone is used.

13.2.2.2 Viral Arthritis

A number of viruses are associated with joint symptoms ranging from arthralgias to true arthritis. These include chikungunya virus, parvovirus B19, hepatitis B and C virus, and rubella, among others. Viral infections typically cause oligoarthritis or polyarthritis. Fever as well as other symptoms typical for each virus can be present as well.

13.2.3 Prosthetic Joint Infections

Prosthetic joint infections occur in about 1–2% of prosthetic joints [7]. They can occur in the first few months after a joint replacement as a result of wound contamination. Late infections (>12 months after surgery) are often due to hematogenous seeding. Prosthetic joint infections are commonly caused by organisms such as *Staphylococcus aureus* and *Streptococcus* species, but other bacteria such as aerobic gram-negative rods and more indolent bacteria such as coagulase-negative staphylococci, diphtheroids, and *Cutibacterium acnes* (Table 13.5) can be involved.

The clinical presentation is similar to native joint arthritis (pain, erythema, and swelling of the involved joint); other clinical aspects of these infections are addressed in Chap. 14.

Table 13.6 lists the causes of prosthetic joint infections.

The diagnosis of prosthetic joint infections can be challenging. Analysis of the synovial fluid is again the main mode of diagnosis. The WBC in the synovial fluid can be much lower compared to native joint infections and a WBC of higher than ~2000 WBC/uL or >65% neutrophils is concerning for an infection. Furthermore, gram stain and synovial fluid culture are not as sensitive and cultures are negative in up to 50% of cases. Multiple tissue samples should be sent during surgical debridement (at least 4–6), which increases the yield of identifying the causative microorganism.

Management of prosthetic joint arthritis depends on a number of different factors, including timing after arthroplasty, organism involved, and presence of joint instability or sinus tracts. Generally, the highest success rates are seen with a two-step joint revision plus antibiotics, but in some cases one-step revision or surgical debridement with liner exchange and retention of the prosthesis may be an option. Antibiotics are typically given for 6 weeks, often intravenously, depending on the pathogen. If the joint is not completely removed, this initial course is

Table 13.6 Causes of prosthetic joint infections

Bacteria
Staphylococcus aureus
Coagulase-negative staphylococci
Streptococcus spp.
Gram-negative bacilli
Cutibacterium acnes
Diphtheroids

Table 13.7 Examples of antibiotic regimens for prosthetic joint infections

Organism	Antibiotics
Methicillin-sensitive *Staphylococcus aureus*	Cefazolin or oxacillin × 6 weeks (plus rifampin if hardware retention)
Methicillin-resistant *Staphylococcus aureus*	Vancomycin × 6 weeks (plus rifampin if hardware retention)
Coagulase-negative staphylococci	Vancomycin × 6 weeks
Streptococcus spp.	Ceftriaxone or penicillin G × 6 weeks
Cutibacterium acnes	Penicillin G or ceftriaxone × 6 weeks
Diphtheroids	Vancomycin × 6 weeks

followed by several months of oral antibiotics and sometimes lifelong suppression.

Table 13.7 lists examples of antibiotic regimens for prosthetic joint infections.

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14 Principles of Musculoskeletal Infections

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Contents

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Goals and Objectives

- *Goal:* To familiarize the reader with infectious diseases of bones and joints and their pathogenesis, bacteriology, morbid anatomy, clinical course, and complications.
- *Objectives:* Upon completion of this unit, the learner should be able to describe, list, or identify the following:

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1. Routes of infection of bones and joints
2. Cellular responses to infection
3. Differences between pediatric and adult populations with regard to musculoskeletal infections
4. Pathogenesis of acute and chronic osteomyelitis
5. Complications of osteomyelitis and septic arthritis
6. Diagnosis of osteomyelitis and septic arthritis
7. Medical and surgical treatment of osteomyelitis and septic arthritis
8. Diagnosis and management of prosthetic joint infections

14.1 Osteomyelitis

14.1.1 Overview

14.1.1.1 Definition

Osteomyelitis is an infection of the bone. It is typically bacterial, most often caused by aerobic or anaerobic bacteria; however, in certain cases it may also be mycobacterial (e.g., disseminated tuberculosis) or fungal in nature [1].

14.1.1.2 Immune Response

Osteomyelitis is similar to other infections with regard to the immune response stimulated by pathogenic organisms, including innate and adaptive immune responses. These will not be covered in detail here. The architecture of the bone produces certain obstacles to an effective immune response. Microscopic channels and trabecular spaces within the bone prevent immune cells from accessing pathogens and eradicating them.

14.1.1.3 Bone Response

Part of the body's response to infection of the bone is resorption of the bone via the action of osteoclasts. This is favorable for facilitating access by immune cells to pathogenic organisms, but it also produces the unwanted effect of weakening bone, leading to collapse or pathologic fracture. The body also responds by producing new bone around the areas of infection, which can lead to coexistence of dead, chronically infected bone (referred to as a sequestrum), encased in new, immature bone (referred to as the involucrum). The presence of chronically infected dead bone encased in new bone further prevents access of immune cells and antibiotics to pathogenic organisms.

14.1.1.4 Routes of Infection

Pathogenic organisms may enter the bone by way of three common routes: (1) they may be spread hematogenously from another locus of infection, (2) they may be introduced directly into the bone via trauma (e.g., open fractures or surgery), or (3) they may be spread directly from infections of adjacent tissue.

14.1.2 Hematogenous Osteomyelitis

14.1.2.1 Pathogenesis

Transient bacteremia occurs on a daily basis from a variety of sources such as minor infections, minor trauma to the skin, or even dental procedures. Bacteria are typically cleared from the bloodstream by the immune system, but if they are able to establish a focus of infection within the bone, osteomyelitis may develop [2].

14.1.2.2 Bacteriology

The bacteriology of these infections is covered in Chap. 13.

14.1.2.3 Pathology

In children, the unique anatomy of the microvasculature of the bone permits bacteria to establish infection preferentially in the metaphysis [2]. Bacteria enter the bone through the larger nutrient arteries and traverse the vascular channels within the bone distally and proximally into steadily smaller vessels. As these vessels approach the metaphysis, the caliber decreases down to capillary level, and at the epiphyseal (growth) plate the small-caliber vascular channels must make a one hundred eighty degree (180°) turn to carry now venous blood back out of the bone via the nutrient

veins. Due to the caliber and course of the vascular channels at the level of the epiphyseal plate, bacteria can easily become lodged in the metaphysis just proximal to the physis. If they become lodged in this area, the immune system cannot readily access them, and bacterial replication may outstrip the immune response and lead to a focus of infection. The damage caused to the surrounding tissues and thrombosis caused by the bacteria themselves and by the innate immune response further prohibit the immune system from accessing the developing infection. The growing infection spreads within and between adjacent vascular channels. Due to the constrained nature of these channels, the pus formed by the rapidly replicating bacteria and by the numerous immune cells attempting to control the infection spreads proximally up the metaphysis and diaphysis of the bone. In children, the physis typically prohibits the spread of the infection into the epiphysis, though in infants (under 1 year of age) some vascular channels traverse the epiphyseal plate and infection may spread in both directions from metaphysis (into both the epiphysis and diaphysis). Expanding infection that permeates the cortical bone is then trapped by the dense fibrous capsule present around growing pediatric bone. There are several anatomic locations in which a physis is intra-articular, leading to early development of adjacent septic arthritis, discussed in more detail below. These locations are the hip, shoulder, elbow, and ankle.

Pus that has permeated the cortex remains pressurized and dissects the periosteum from the adjacent cortex, spreading along the surface of the bone. This spread of pus between the periosteum and bone devascularizes the bone. Bones receive both endosteal and periosteal blood supply, both of which are disrupted in osteomyelitis by the spread of bacteria within the vascular channels in the medullary cavity and within the periosteum. If the bone is sufficiently devascularized, the cellular components (osteoblasts, osteoclasts) will undergo necrosis, leaving on the acellular matrix of proteins and hydroxyapatite with empty channels and lacunae. These areas of dead bone are havens for bacteria, and a segment of dead bone filled with and surrounded by pus is referred to as a *sequestrum*.

The inflammatory response to the infection stimulates rapid formation of new woven bone by osteoblasts. This bone is laid down as the body's attempt to stabilize the weakened extremity. In severe cases, the entire diaphysis of the bone may become a sequestrum encased in a circumferential involucrum. An opening in the involucrum is referred to as a cloaca and allows pus to drain into the surrounding soft tissues. The drainage can penetrate the skin through sinus tracts. These tracts can complicate treatment and make adequate local debridement more challenging.

In adults the vascular anatomy of the bone differs as the epiphyseal plates have closed. In addition, the most common site of hematogenous osteomyelitis is vertebral bodies due to bacterial seeding from IV drug use or pelvic causes such as gynecologic or urologic infection or surgery and bacteria within pelvic venous plexuses. This can lead to collapse of the spinal column, epidural abscess, and spinal cord injury.

14.1.2.4 Radiographic Manifestations

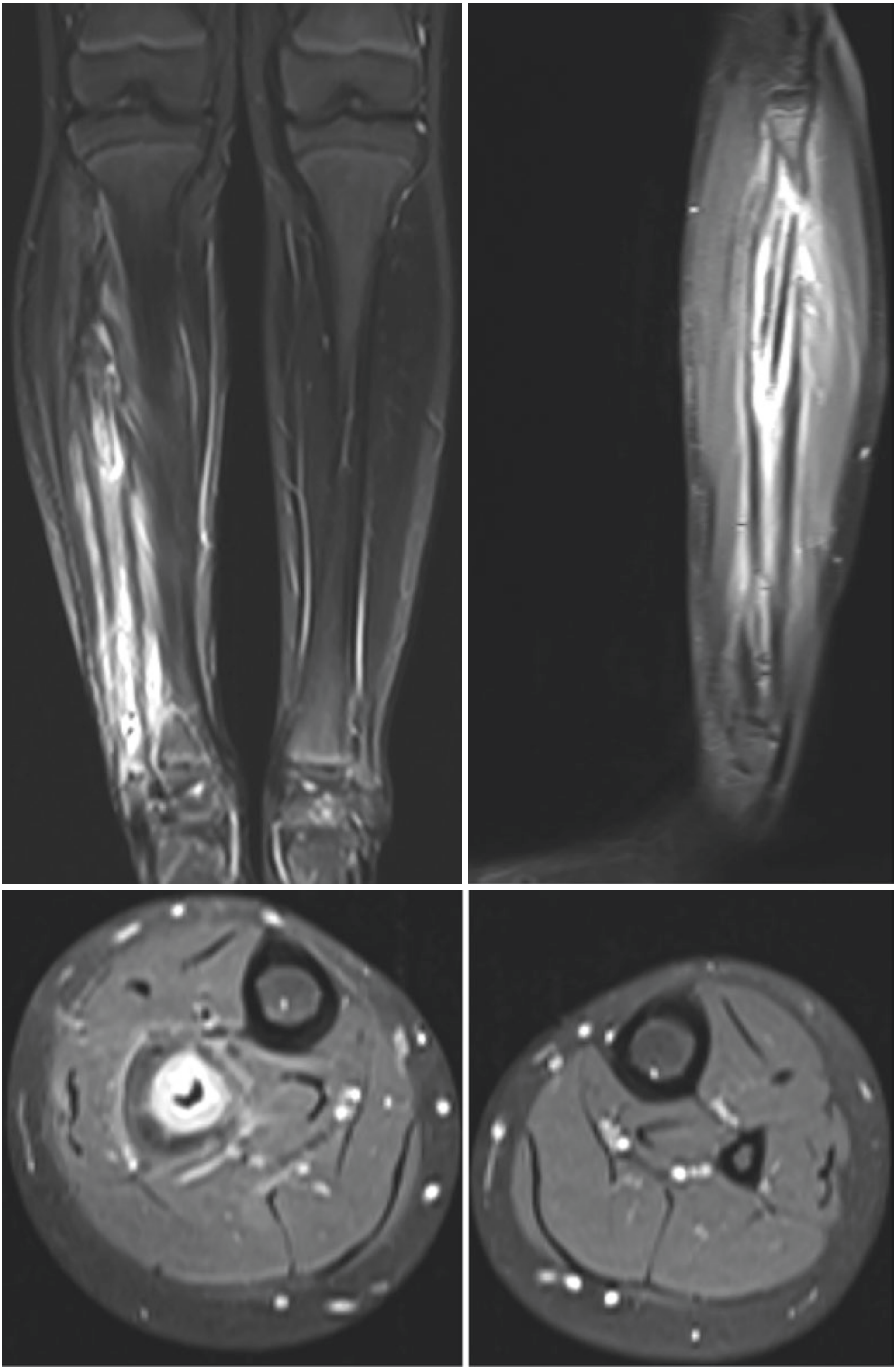
Radiographic images can show some of the soft tissue effects of osteomyelitis such as swelling and in aggressive infections subcutaneous gas. However, the bony features of osteomyelitis are not apparent for at least 1–2 weeks after infection has been established. The first noticeable radiographic feature that suggests osteomyelitis is resorption of the bone causing lucency in the affected area. This is caused by the inflammatory response and increased osteoclast activity [3].

Radiographically apparent new bone formation is typically first noted as a *periosteal reaction*, often in the metaphyseal region first then extending along the diaphysis if the infection is extensive. This is the new bone that may progress to form an involucrum in cases where the infection is not cleared and chronic osteomyelitis develops.

Finally, if a sequestrum develops, the dead, infected bone is typically sclerotic (or more radiopaque than the normal healthy bone). The sclerotic sequestrum is typically surrounded by a lucent margin of bacteria, inflammatory cells, and granulation tissue, which is all encased in involucrum (Figs. 14.1 and 14.2). In some cases, a well-circumscribed lytic lesion can be seen, representing a *Brodie's abscess*, described below.

Figs. 14.1 and 14.2 Anteroposterior (AP) and lateral radiographs of a skeletally immature patient with extensive chronic osteomyelitis of the fibula. Note the "bone within bone" appearance of the sequestrum (central necrotic bone) surrounded by periosteal, reactive new bone (involucrum)

A radioisotope bone scan utilizing technetium or gallium can show hypermetabolic areas consistent with osteomyelitis prior to the development of radiographically apparent lucency around 1–2 weeks [2]. While plain radiographs are essential in the evaluation of patients with osteomyelitis, magnetic resonance imaging (MRI) is essential in defining the extent of involvement (Figs. 14.3, 14.4, and 14.5).



Figs. 14.3, 14.4, and 14.5 MRI images from the patient shown in Figs. 14.1 and 14.2. Note the extensive bright signal on these T2-weighted images. MRI is superior to plain radiographs at delineating the extent of intraosseous involvement

Fig. 14.6 Lateral radiograph of a patient with an intraosseous (Brodie's) abscess of the proximal tibia. Note the lucency in the posterior aspect of the bone

MRI can also show areas of increased T2 signal (essentially showing free water or edema) and enhancement if gadolinium contrast is used, also raising suspicion for osteomyelitis. Both of these are, however, nonspecific and can be signs of other non-infectious processes such as neoplasm.

14.1.2.5 Clinical Course

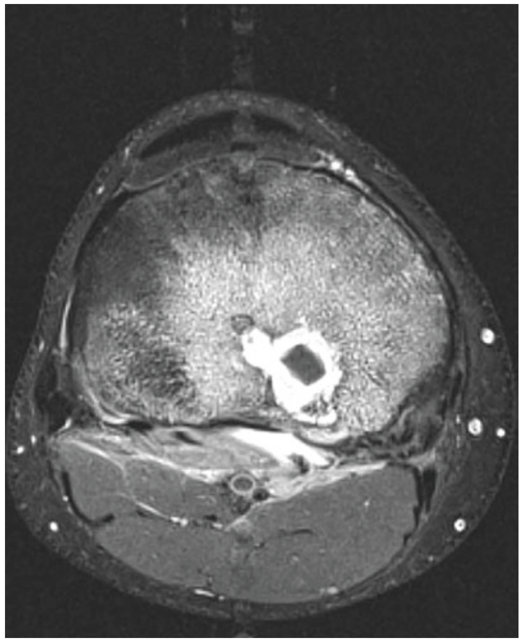
Most common foci of hematogenous osteomyelitis are areas of rapid epiphyseal growth including the distal femur, proximal tibia, and proximal humerus, among others. History and physical may elucidate a source of bacteremia that gave rise to the infection, such as cellulitis, dental infection, respiratory tract infections, or urinary tract infections, but in many cases the source is unknown. The history may also be notable for minor trauma such as an ankle sprain, which is typically only temporally related to the onset of infection but may be a red herring that delays diagnosis.

Symptoms of acute osteomyelitis are similar to those of other acute infections, including fever, pain, erythema, warmth, and swelling. Laboratory markers are also those used for other infections such as the serum white blood cell count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and blood cultures.

Pain and tenderness are usually localized at the onset of an infection. As the infection progresses, however, inflammation becomes more diffuse along the involved portion of bone. Clinical symptoms, inflammatory laboratory markers, and imaging can all be used to assess response to treatment.

Untreated osteomyelitis can lead to significant morbidity including bacteremia, multiple foci of infection due to hematogenous spread, and septicemia. If treated promptly with appropriate antibiotics (initially empiric then based on cultures and susceptibilities), the infection may be cleared and the damage to the bone may remain limited and recover fully with time. However, if not adequately treated, chronic infection may develop and the above-described sequestrum will harbor dormant infection that is not accessible to the immune system or systemic antibiotics.

In some cases, the immune response successfully walls off the infection within the metaphysis, forming a capsule of inflammatory and fibrous tissue around the focus of bacteria. This forms an intraosseous abscess known as a Brodie's abscess (Figs. 14.6, 14.7, and 14.8). The bone around the abscess may be dense and sclerotic with radiolucent pus and soft tissue within the cavity. It may be weakened by infection and by the resultant inflammatory response, predisposing the bone to pathologic fracture (or fracture due to a low-energy mechanism that would not overcome the strength of a healthy bone).



Figs. 14.7 and 14.8 MRI images of an intraosseous abscess. In Fig. 14.8, note the post-contrast appearance on this transverse (axial) image. On post-contrast imaging, the abscess will show enhancement of the periphery but not the central, necrotic, avascular aspects of the lesion. This kind of "rim enhancement" is typical of cystic or fluid-filled biologic processes

This type of injury may be the presenting sign of osteomyelitis with a history notable for prodromal pain, fever, redness, and other symptoms as described above.

14.1.2.6 Complications

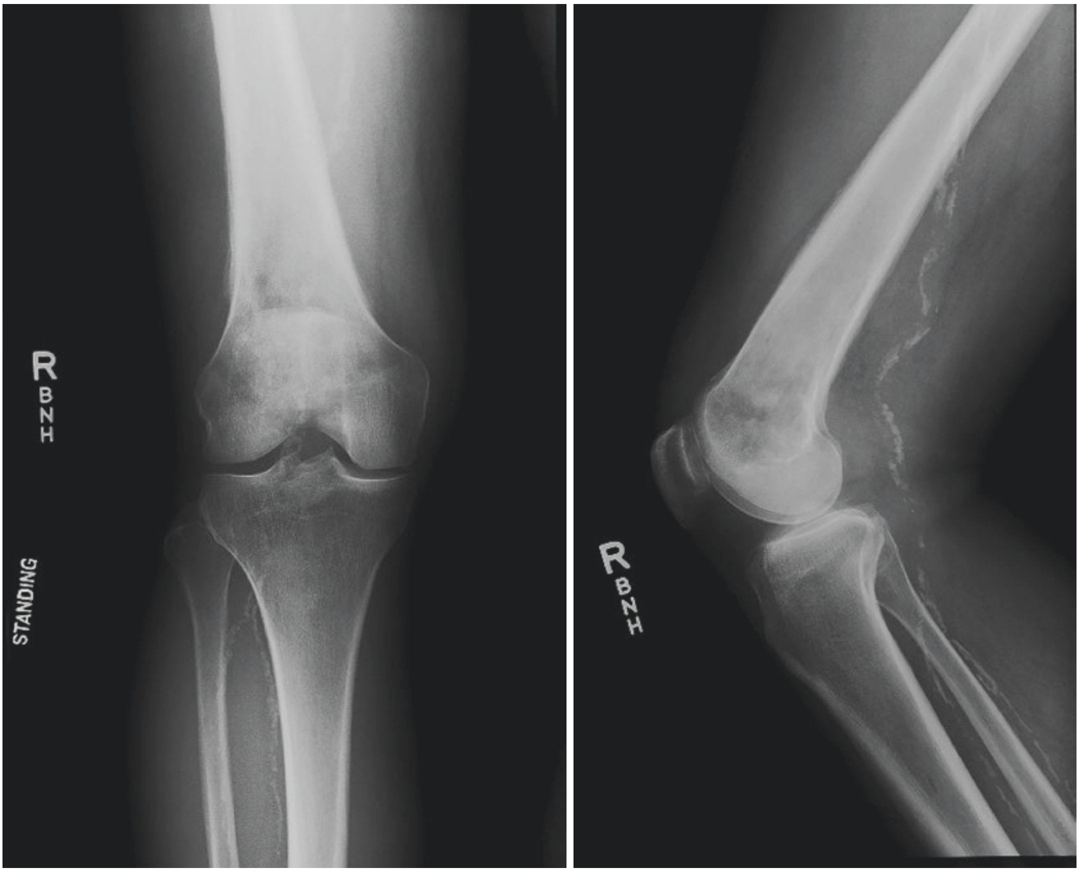
There are numerous complications of untreated and treated osteomyelitis. Some of these complications have been described above including local damage to the bone, pathologic fracture, adjacent septic arthritis (typically in hip or shoulder in pediatric patients due to the anatomy described above, or in any joint in adults with closed growth plates) (Figs. 14.9, 14.10, and 14.11), Brodie's abscess, sequestrum formation, draining sinus tracts, systemic illness.

Other complications include chronic inflammation and cell turnover at sites of draining sinus tracts leading to repetitive mutations and malignant transformation of skin cells. Development of squamous cell carcinoma can occur at sites of draining sinus tracts and is referred to as *Marjolin ulcer*.

In adults, vertebral body osteomyelitis may lead to spinal column, epidural abscess, and spinal cord injury as mentioned above.

14.1.2.7 Treatment

Initial treatment of acute osteomyelitis is appropriate antibiotics. Initially antibiotics are empiric and based on clinical suspicion for the causative organism as outlined above in bacteriology [4]. Subsequently, they are tailored to the pathogenic organism based on cultures from blood or surgical debridement and susceptibility testing. Antibiotics may be necessary but not sufficient for successful infection treatment. If there is nonviable tissue with poor vascularity, even parenteral antibiotics will not be enough to clear an infection. If fulminant or chronic infection develops with sequestrum formation or intraosseous abscess, surgical debridement is usually necessary to optimize the likelihood of clearing the infection.



Figs. 14.9 and 14.10 AP and lateral radiographs of a 68-year-old man with chronic osteomyelitis of the femur. Note the extensive, mixed lucent, and dense changes within the bone. In this patient, there was initial concern for neoplasm (lymphoma). Note also the extensive vascular calcifications in this diabetic patient

14.1.3 Exogenous Osteomyelitis

14.1.3.1 Etiology

The distinguishing factor between hematogenous and exogenous osteomyelitis is the route of infection and therefore the clinical scenarios that give rise to it. Exogenous osteomyelitis results from direct contamination of the bone from the environment. This occurs in open (once commonly referred to as "compound") fractures; diabetic, vasculopathic, and decubitus ulcers; foreign bodies such as nails, splinters, and ballistics (bullets, shotgun pellets); and post-operative infections.

The degree of damage to the bone and soft tissue envelope determines whether osteomyelitis will develop following a given insult. Extensive soft tissue stripping, contamination with soil or stool, larger wounds, and vascular injury all increase the risk of infection after open fractures. Host factors also determine the resilience to infection. Immunocompromised (intrinsically via genetic defect or AIDS or iatrogenically secondary to steroids or other immunomodulators), diabetic, vasculopathic, or polytraumatized patients are more likely to develop infection.[6] More virulent organisms such as those covered above in bacteriology and often found in stool and soil are more likely to cause osteomyelitis. For this reason, barnyard injuries and crush injuries with extensive soft tissue damage and gross contamination are some of the highest risk injuries.

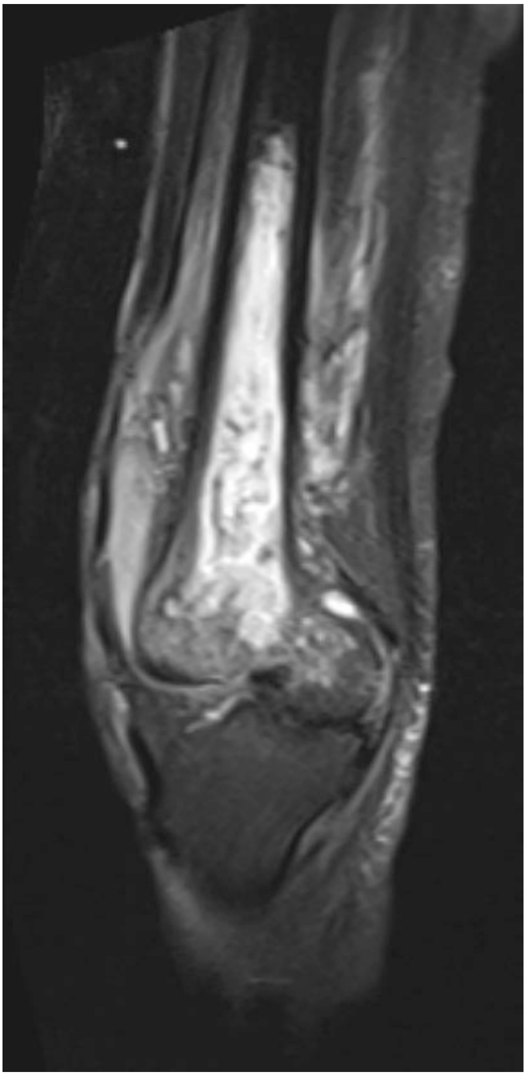


Fig. 14.11 T2-weighted MRI image of the same patient. Note the considerable marrow involvement with proximal and distal extension of the infection

14.1.3.2 Pathology

Exogenous osteomyelitis rarely spreads beyond the site of inoculation, but it very quickly becomes chronic due to the presence of dead or devascularized bone from comminuted open fractures, soft tissue stripping, retained foreign material, or ballistic injury. Multiple small sequestra and abscess often form, making cure even with extensive debridement difficult. This is further complicated by the frequent necessity of stabilizing implants such as plate and screw constructs or intramedullary nails in spite of known contamination or even known infection. This is covered in more detail below.

14.1.3.3 Clinical Course

Following a traumatic injury or procedure as described above, increasing pain, erythema, drainage, purulence, fluctuance, and fever are all concerning for deep infection such as osteomyelitis. Following initiation of appropriate antibiotics, systemic illness and sepsis are very uncommon, but local infection is exceedingly hard to eradicate for the reasons outlined above (soft tissue injury, devascularized bone, retained foreign material). This leads to chronic osteomyelitis with features as described above. In severe cases, the extensive debridement and implant exchange required to attempt cure of chronic osteomyelitis leads ultimately to amputation of the affected extremity at a level above the injury where healthy tissue can successfully heal.

14.1.3.4 Fracture and Implant/Hardware Infection

Open fractures often require plate and screw or intramedullary nail fixation, and other orthopedic procedures such as osteotomies for deformity correction and spinal fusions require permanent implants to stabilize the skeleton. Development of post-traumatic or post-operative infection in this setting leads to a common clinical scenario of known infection with indwelling hardware. Infection also leads to delayed healing (*union*) of fractures of osteotomies/fusions, prolonging the necessity of orthopedic hardware. The treatment of such cases is complex and often requires multiple surgeries and extensive debridement with prolonged courses of intravenous antibiotics. Removal of hardware may be required to clear the infection due to biofilm formation on the metallic surfaces, but this cannot be safely performed until fractures have united or iatrogenic fusions have healed. Hardware exchange is common with removal of contaminated implants, extensive debridement, and replacement with new, in some cases, antibiotic-impregnated implants.

14.2 Septic Arthritis

14.2.1 Etiology

Septic arthritis, also known as infectious, suppurative, or pyogenic arthritis, is an infection within the synovial capsule of a joint. The organism may be introduced via hematogenous spread or by extension from adjacent osteomyelitis as described above, or it may be directly introduced by a traumatic arthrotomy (opening or violation of the joint) or surgical procedure [1]. This section will cover only native joint infections, with prosthetic joint infections covered separately in the next section.

14.2.2 Bacteriology

The bacteriology of these infections is covered in Chap. 13.

14.2.3 Pathogenesis

As with the causes of osteomyelitis, infection of joints may be caused by hematogenous spread from another anatomic site. Joint infection may also occur due to direct inoculation (e.g., traumatic arthrotomy). Bacterial replication within the joint prompts a robust inflammatory response from the synovium and massive chemotaxis of white blood cells (specifically neutrophils) into the joint, with a concomitant painful effusion. The infection and resulting immune response can lead to irreversible damage to articular cartlage in the affected joint. The bone can also destroyed in severe cases by increased vascularity and resorption by inflammatory cells and osteoclasts. Even with effective treatment, this leads to early degenerative disease and arthritis, but if treatment is not initiated promptly, it will lead to complete destruction of the joint.

14.2.4 Clinical Features

Septic arthritis is most commonly monoarticular. It preferentially affects the joint around rapidly growing intra-articular physes in children such as the hip and knee. Gonococcal arthritis may be mono- or polyarticular. As with all infections, immunocompromised hosts are at increased risk of developing septic arthritis. Onset is typically quite fulminant with fever, severe pain, inability to bear weight, effusion, and restricted range of motion (classically the hip in children is held in flexion, abduction, and external rotation as this relaxes the joint capsule). Laboratory markers include WBC count, ESR, and CRP as in other musculoskeletal infections including osteomyelitis. Radiographically, destruction of the cartilage can be inferred from joint space narrowing, and the effusion itself is often visible. Erosion of adjacent bone and osteopenia can also be seen in some cases. MRI is very sensitive for the detection of synovitis and an associated effusion (Fig. 14.12). Bone scans may also show hypermetabolic joints but are used less commonly since MRI became readily available. They are also nonspecific and can show increased uptake in sterile degenerative processes such as osteoarthritis and inflammatory processes such as rheumatoid arthritis [2].

Fig. 14.12 T2-weighted MRI image of a 47-year-old man with septic arthritis of the knee. Note the large joint effusion and edematous peri-articular tissues

14.2.5 Diagnosis

Septic arthritis is a surgical emergency, so clinical suspicion for it must trigger immediate arthrocentesis (aspiration of joint fluid), which should be sent for analysis, specifically nucleated cell count and crystal analysis (as crystalline arthropathies such as gout and pseudogout are often on the differential). Fluid is also sent for gram stain and culture, though this is less helpful acutely than the synovial WBC (nucleated cell) count. The cutoff commonly used for diagnosis of septic arthritis is 50,000 WBCs per mL, typically with >50% neutrophils. In patients with fewer than 50 K cells, sterile inflammatory processes such as gout and rheumatoid arthritis are most common, while above 50 K cells septic arthritis is presumed.

14.2.6 Treatment

Treatment is based on prompt irrigation debridement with an arthrotomy and debridement of unhealthy synovium and initiation of appropriate antibiotics. Broad-spectrum antibiotics are initiated empirically then narrowed based on culture and sensitivity data [5]. In patients too sick or unstable to undergo surgery, serial aspiration and injection of intra-articular antibiotics may be used as a second-line therapy. While the joint recovers, it is often immobilized to protect the damaged synovium and cartilage.

14.2.7 Complications

Complications of untreated infection include destruction of the joint, sepsis, and potentially death. However, with prompt treatment systemic effects are typically mitigated and the complications are limited to early degenerative disease from damage to cartilage, ligaments, and bone. Some patients with persistent infection can go on to develop chronic osteomyelitis (Fig. 14.13).

Fig. 14.13 T2-weighted MRI image of a patient with chronic knee infection that led to osteomyelitis. Note the abundant amount of reactive synovial tissue and extensive osseous involvement

14.3 Prosthetic Joint Infection

14.3.1 Etiology

Infection is one of the most devastating complications of joint replacement. Prosthetic joints place metal and plastic in an immunologically privileged capsule, making them highly susceptible to infection which is particularly difficult to eradicate. Prosthetic joint infection (PJI) may occur immediately following total joint replacement as a post-operative infection or at any time later, even years or decades following surgery and complete healing. Late infection is typically due to hematogenous seeding from even minor sources of bacteremia such as dental procedures. Some providers advocate antibiotic prophylaxis for dental procedures due to the risk of PJI. Risk of PJI is increased by other infections at the time of surgery, even minor cutaneous infection, as well as by history of prior surgery on the affected

joint. It is also intuitively elevated in immunocompromised patients and patients with poorly controlled diabetes [5].

14.3.2 Bacteriology

The most common organisms in PJI are *S. aureus* in acute, fulminant infection, *S. epidermidis* and other coagulase-negative *Staphylococcus* spp. in more indolent chronic infections, and a slow-growing organism called *Propionibacterium acnes* in subacute and chronic infections. *P. acnes* often takes many weeks to grow on cultures from joint aspirate or surgical debridement, so prosthetic joint cultures should be kept for 6 weeks before being considered final negative.

14.3.3 Clinical Features

Unusually persistent or recurrent pain following joint arthroplasty raises concern for infection. More concerning signs are peri-incisional erythema, drainage, effusion/swelling, and fever. A chronically draining sinus over a prosthetic joint even in the absence of any other clinical information is pathognomonic for prosthetic joint infection. Elevated inflammatory markers such as WBC, ESR, and CRP raise suspicion as with other infections.

14.3.4 Diagnosis

Diagnosis of PJI can be complex, but synovial fluid analysis is the cornerstone. Joint aspirate should be sent for culture (kept for 6 weeks as above) and for nucleated cell count and differential. In the first 6 weeks following surgery, cell count is normally elevated due to the inflammatory phase of healing, but elevation beyond 30,000 is concerning for PJI. Beyond 6 weeks post-operatively, a cell count below 1100 is reassuring, a cell count between 1100 and 3000 is indeterminate, and a cell count above 3000 is diagnostic of PJI. Alpha defensin is a new assay that is specific for WBCs in the presence of bacteria which can be used as an adjunct when other testing is inconclusive.

14.3.5 Treatment

Acute infection within 3 weeks of surgery may be treated with surgical irrigation and debridement with exchange of the polyethylene liner of the prosthetic joint only, followed typically by 6 weeks of IV antibiotics. Established infection is a very difficult problem and typically necessitates two-stage exchange arthroplasty with removal of all components and cement, placement of antibiotic spacer in the defect where the prosthetic joint was removed, 6 weeks of IV antibiotics, conclusive evidence that infection has been eradicated, and revision arthroplasty following clearance of infection, which is always more involved and morbid than primary arthroplasty.

14.3.6 Complications

The primary complications are the significant morbidity and mortality risk of multiple surgeries. Systemic illness is uncommon as a result of PJI but can occur. PJI that goes undiagnosed can cause extensive, irreparable bone loss, complicating and potentially preventing future reconstruction and leading to debility.

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15 Vascular Disorders of Bone

Joshua A. Shapiro

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the principles of pathogenesis, diagnosis, and treatment of ischemic necrosis, osteochondrosis, and hemophilic arthropathy.
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe, list, or identify:
  1. The presentation, pathogenesis, and differential diagnosis of avascular necrosis, osteochondrosis, hemarthrosis, and soft tissue hematoma
  2. Ten etiologies of avascular necrosis using the "ASEPTIC" acronym
  3. Three possible mechanisms for the pathogenesis of avascular necrosis

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4. Imaging findings and general treatment guidelines for avascular necrosis, osteochondrosis, hemarthrosis, and hematoma

15.1 Understanding Avascular Necrosis

Avascular necrosis of bone (AVN) is defined as a massive necrosis of bone and marrow occurring as the primary abnormality. Secondary forms of AVN can be seen in severe forms of osteoarthritis, fractures, neoplasms, and infections; however, this secondary necrosis does not fall under the umbrella term "avascular necrosis." AVN is caused by a disruption in blood supply, resulting in a characteristic pattern of osteocyte death, bone remodeling, subchondral collapse, and arthrosis. The primary cause of AVN is *ischemia*, first to marrow adipocytes and hematopoietic cells and then to the osteocytes. Long bone epiphyses such as the humeral and femoral heads are prone to ischemia due to watershed vascular zones.

A good history is essential when AVN is considered, as understanding the primary insult can help the clinician in counseling the patient and avoiding future occurrences. The differential of etiologies is extensive, but can be readily recalled with the "ASEPTIC" acronym: *a*lcohol, *a*cquired immunodeficiency syndrome, *s*teroids, *s*ickle cell disease, *s*ystemic lupus erythematosus, *E*rlenmeyer flask (Gaucher's), *p*ancreatitis, *t*rauma, *i*nfection, *C*aisson's. Despite this extensive differential, the cause of osteonecrosis is idiopathic in up to 25–50% of cases [1, 2]. The pathogenesis of AVN among this wide array of etiologies will be examined in the following subsections.

15.2 Pathophysiology of Avascular Necrosis

AVN is characterized by a reproducible pattern of cellular necrosis with a net imbalance in resorption and formation yielding structurally weaker bone prone to collapse [3]. Ischemia yields necrosis in marrow adipocytes and hematopoietic cells before spreading to other osteocytic lineages. Osteocytes suffer necrosis within 2–3 h of anoxia [4]. A bone remodeling process called *creeping substitution* ensues where osteoclastic resorption and creation of new vascular channels enable osteoblastic bone formation. However, ischemia renders creeping substitution incomplete, reducing osteoclastic activity and enabling osteoblasts to laminate the new bone to sclerotic bone. This yields a weakened architecture in the epiphysis that is susceptible to fracture and collapse, ultimately accelerating arthritis [3, 5] (Fig. 15.1).

The known pathophysiologic mechanisms of AVN are (1) traumatic vascular interruption, (2)

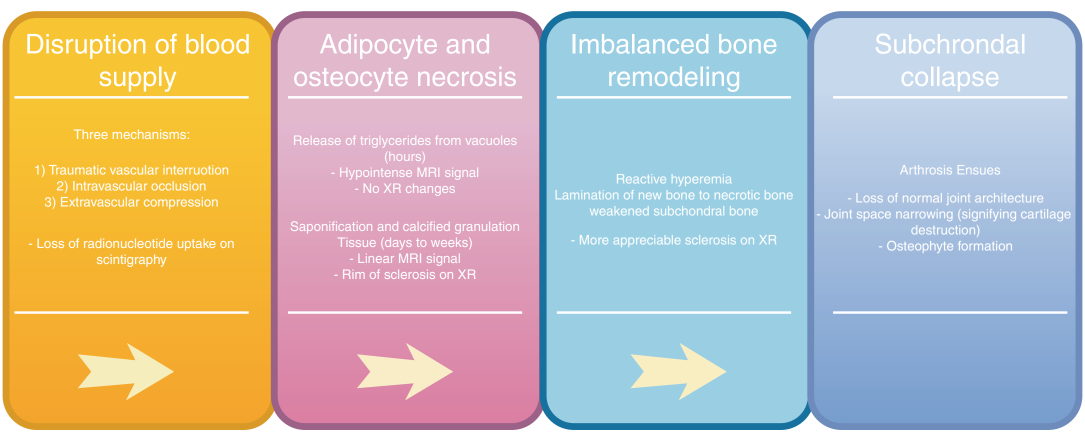

Fig. 15.1 Diagram of the pathogenesis of avascular necrosis. Disruption of blood supply results in adipocyte necrosis followed by osteocyte necrosis. An imbalanced bone remodeling, by a physiologic process called "creeping substitution," yields a weakened architecture that may collapse resulting in arthritis

intravascular occlusion, and (3) intraosseous extravascular compression.

Traumatic Vascular Interruption Fractures and dislocations may cause direct trauma to vessels that supply the bone rendering it at risk for AVN. Prior studies have shown a direct correlation between the number of vessels that cross a fracture or dislocation, the degree of displacement, and the degree of malreduction and the incidence of AVN [6–8]. Hence, the more vessels at risk, the more displaced the initial injury, and the more malreduced a fracture or dislocation is after reduction or fixation correlate with an increased risk of AVN.

Intravascular Occlusion Sickle cell disease and various thrombi including blood clot, fat, and air have been reported to occlude osseous vascular systems in the pathogenesis of AVN. In sickle cell disease, reduced oxygen tension triggers hemoglobin precipitation, which in turn causes sickled cells that adhere to one another and obstruct microvasculature [9, 10]. It is possible for patients with sickle cell disease to have bilateral or polyarticular pathology, and the risk of this increases with patient age [11]. Inherited thrombophilia such as protein C and S deficiency, antithrombin III deficiency, and protein C resistance have been shown to occlude vasculature resulting in AVN [12]. In fact, acquired thrombophilia has been found in up to 82% of patients with AVN compared to just 30% of unaffected controls [12, 13]. In pancreatitis, systemic release of trypsin, a proteolytic enzyme, may result in endothelial damage leading to thrombus formation [14]. Finally, Caisson disease produces occlusive nitrogen gas bubbles upon depressurization amid ascent from a deep sea dive [2].

Intraosseous Extravascular Compression External compression of intraosseous vasculature can reduce blood flow and produce AVN. Drugs and medications including alcohol and corticosteroids have been implicated in adipocyte hypertrophy, altered lipid metabolism, and the shunting of stem cells from an osteocytic to an adipocytic lineage, in turn increasing intraosseous pressure [15, 16]. The risk of AVN may increase by a factor of 4.6 and 9.8 for daily consumption of 10 mg corticosteroid and 400 mL alcohol, respectively [17, 18]. Evidence of AVN may show as early as 1–6 months after exposure to alcohol or corticosteroids [2, 19]. Corticosteroids are commonly used to treat inflammatory conditions such as systemic lupus erythematosus and rheumatoid arthritis [2]. Gaucher disease is an inherited disorder of glycogen storage in which beta-glucocerebrosidase deficiency results in large amounts of lysosomal glucocerebrosidase that increases intraosseous pressures [20]. Other lysosomal storage disorders, including mucopolysaccharidoses, have been implicated in AVN via a similar pathogenesis [21].

To round out the ASEPTIC acronym, HIV/AIDS has an unclear mechanism in the pathogenesis of AVN; however, concomitant risk factors, such as those just described, are likely to contribute [2].

15.3 Avascular Necrosis Throughout the Musculoskeletal System

Hip The femoral head is the most common place for AVN to present from both systemic (think ASEPTIC) and post-traumatic etiologies [2]. Patients with femoral head AVN may present with groin or anterior thigh pain that is worse with stairs, inclines, and impact. An antalgic gait (shortened stance phase on the affected side) is often appreciated. On physical examination, pain may be elicited with flexion, adduction, and internal rotation (FADIR) as well as resisted hip flexion (Stinchfield). The femoral head is at risk for post-traumatic AVN due to its retrograde blood supply from the deep branch of the medial circumflex femoral artery [14]. This artery enters the proximal femur from within the hip joint capsule, portending a high risk of AVN after

Fig. 15.2 Plain x-ray of a right hip with avascular necrosis pre-collapse. Note the rim of sclerosis demarcated by the arrow in the femoral head and the congruent articulation

intracapsular femoral neck fracture and femoroacetabular dislocation [6, 14, 22, 23]. Extracapsular fractures are distal to the arterial entry and are at near-negligible risk of AVN [14]. Treatment is aimed at preserving the existing articulation or, if subchondral collapse has already occurred, then resurfacing or replacing the joint. Although medical therapies including bisphosphonates have been proposed for pre-collapse AVN, their utility is controversial [24–26]. Rather pre-collapse (Fig. 15.2) AVN in the femoral head is amenable to core decompression, a procedure in which a drill is advanced into the sclerotic bone, relieving intraosseous hypertension and stimulating angiogenesis to promote creeping substitution [27–29]. Rotational osteotomy to move the sclerosis away from the weight bearing surface and curettage with bone grafting have also been described for pre-collapse [27, 28, 30]. For those with collapse (Fig. 15.3), total hip arthroplasty or resurfacing is indicated [31, 32].

Shoulder Patients with shoulder AVN may complain of pain, weakness, and reduced or limited range of motion. Physical examination may show point tenderness of the glenohumeral articulation, weakness, strength limited by pain, and diminished range of motion. Shoulder AVN is most commonly caused by corticosteroid use; however, post-traumatic AVN does occur [33]. Although widely debated, recent studies show that two-thirds of the blood supply to the humeral head originates from the posterior circumflex humeral artery, while the anterior circumflex humeral artery supplies the remainder [34]. As in the hip, treatment is dependent upon the structural integrity of the proximal humerus. If a sclerotic lesion is identified pre-collapse (Fig. 15.4), then arthroscopic-assisted core decompression (Fig. 15.5) and bone grafting have had success. However, if collapsed, then arthroplasty, resurfacing, or arthrodesis is indicated [33].

Fig. 15.3 Plain x-ray of a right hip with avascular necrosis post-collapse. Note the rim of sclerosis demarcated by the star, the subchondral fracture demarcated by the arrow, and the loss of articular congruency

Wrist The scaphoid and lunate are commonly implicated in wrist AVN. The scaphoid is at risk for AVN due to its tenuous blood supply from the dorsal carpal branch of the radial artery, which enters the scaphoid dorsally and supplies the proximal 80% of the scaphoid via a *retrograde* flow. Thus, more *proximal* fractures portend a higher risk of compromised blood supply to the *proximal* segment. Patients with AVN of the

Fig. 15.4 Plain x-ray of a left shoulder with avascular necrosis pre-collapse. Note the rim of sclerosis demarcated by the arrow in the humeral head and the congruent articulation

Fig. 15.5 Arthroscopic-assisted core decompression. This is an intraoperative radiograph showing drill bit decompression of sclerosis, using an arthroscope, to ensure the articular cortex is not violated by the drill bit. There are two drill bits entering from the lateral cortex. The arthroscope is positioned medially

scaphoid may complain of weakness, reduced strength in grip and pinch, wrist stiffness, and limited wrist motion. On physical examination, the clinician may find tenderness between the first and third dorsal compartments and at the volar scaphoid tubercle. If untreated, a pattern of arthrosis as seen in scaphoid nonunion advanced collapse (SNAC) may unfold including radial styloid arthrosis, scaphocapitate arthrosis, and pan-scaphoid arthrosis. Treatment is aimed at restoring vascularity with vascularized bone graft, or if arthrosis is present, then resection of the point of arthrosis, for example, with radial styloidectomy and proximal row carpectomy, or arthrodesis is indicated [35].

While the majority of scaphoid AVN is post-traumatic, the majority of lunate AVN is atraumatic. Pathoanatomic features including an unlevel joint where the ulna is shorter than the radius and a variant I-pattern blood supply (rather than Y- or X-pattern) are correlated with lunate AVN, known as Kienbock's disease. The average age of onset of Kienbock's disease is 20–40 years with a male predilection. Patients with Kienbock's disease may complain of dorsal wrist pain worse with activity. Physical examination may show swelling and tenderness over the lunate with decreased arc of flexion and extension and diminished grip strength. The stages of Kienbock's disease are edema followed by sclerosis, collapse, scaphoid rotation, and adjacent intercarpal arthrosis. For those with pre-collapse disease, symptomatic control with immobilization and NSAIDs may be sufficient. Those with an unlevel joint may benefit from a joint-leveling procedure. Vascularity may be restored pre-collapse with core decompression or vascularized bone graft. Once symptomatic collapse or adjacent intercarpal disease is evident, then arthrodesis or proximal row carpectomy is indicated [36].

Knee Knee AVN may be spontaneous or secondary to systemic factors. Spontaneous osteonecrosis of the knee (SPONK) occurs in the middle aged to elderly and affects females more frequently than males. It is predominately monoarticular and usually affects the epiphysis of the medial femoral condyle. The underlying pathophysiology is thought to be a subchondral insufficiency fracture or possibly a meniscal root tear [37]. Patients may present with sudden onset of severe knee pain, effusion, tenderness, and limited range of motion [38]. Secondary osteonecro-

sis of the knee (SONK) is related to systemic factors such as corticosteroid use and thrombophilia. Middle-aged women are more often affected than men. Like other systemic manifestations of AVN (think ASEPTIC acronym), SONK is *not restricted* to just the medial knee and may present bilaterally [39]. Like SPONK, patients present with functional pain, tenderness, and limited range of motion. Both SPONK and SONK are typically self-limiting and remit with nonoperative modalities including analgesia, protected weight bearing, quadriceps strengthening, and activity modification. Operative intervention is reserved for those who failed nonoperative management, including core decompression for extra-articular lesions, osteochondral allograft for younger patients, and total knee arthroplasty for older patients, those with large articular involvement, and those with symptomatic collapse [40].

Ankle The talus is at high risk for avascular necrosis due to its *retrograde*, extra-osseous blood supply and limited soft tissue attachments. The main arterial supply to the talus is the posterior tibial artery via the artery of the tarsal canal, which can be injured in talar neck fractures and tibiotalar and subtalar dislocations. Patients may complain of pain, ankle weakness and instability, and reduced ability to bear weight. The risk of AVN after talar fracture has been reported as 16.6–88% but is less common than post-traumatic arthritis [41]. Treatment of talar AVN includes bracing, protected weight bearing, physical therapy, core decompression, vascularized grafts, arthrodesis, and total ankle replacement depending on the level of necrosis and collapse [42].

15.4 Imaging Findings in Avascular Necrosis

Radiologic evaluation of AVN should begin with plain x-rays of the affected joint to evaluate the bony and articular architecture. However, since marrow adipocytes are the first to become ischemic, scintigraphy and MRI are more sensitive in early stages of disease. Scintigraphy will show reduced tracer uptake as soon as ischemia is apparent. As adipocyte vacuoles rupture instigating saponification, a hypointense MRI signal will be apparent, signifying loss of normal marrow fat and high concentrations of calcification (Fig. 15.6a, b). Physiologic creeping substitution is seen as a serpiginous crescent, demarcating remodeled from sclerotic bone. However, it may take weeks before calcified granulation tissue develops at the interface of healthy and necrotic bone, which can be seen as a hot spot on bone scintigraphy, a linear MRI signal, and finally as an increased opacity on x-ray and CT. Deformed

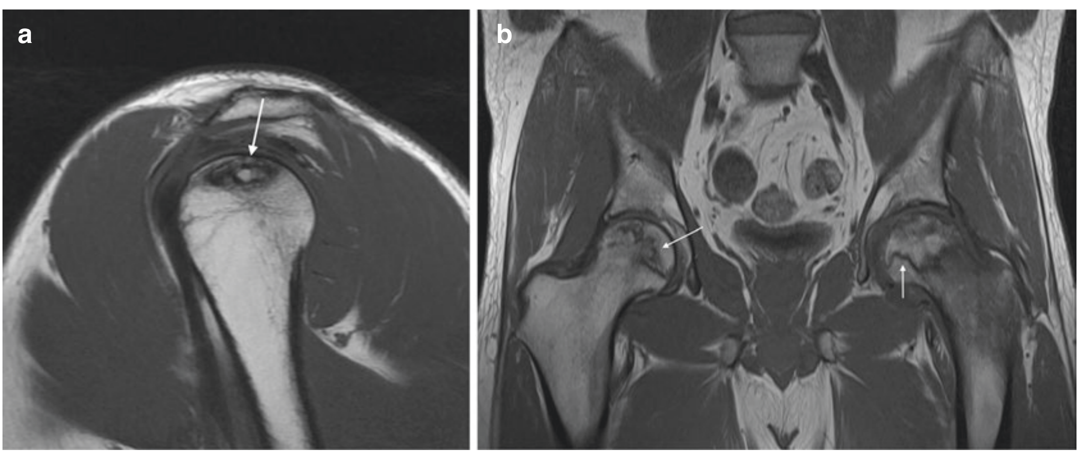

Fig. 15.6 MRI of avascular necrosis. T1-weighted MRI features of avascular necrosis in the (**a**) right humeral head and (**b**) bilateral femoral heads. Note the hypointense signal signifying necrosis and calcification relative to the T1 intense signal of marrow fat. The arrows in (**b**) point to serpiginous crescents, demarcating remodeled from sclerotic bone

and necrotic subchondral bone places substantial stress on the overlying cartilage resulting in delamination, cartilage destruction, and other osteoarthritic changes. The crescent sign, seen on x-ray, is indicative of articular collapse [43].

15.5 Bone Infarct

Bone infarcts have similar etiologies to and are within the same disease spectrum as AVN; however, rather than afflicting long bone epiphyses, bone infarcts occur within the metadiaphysis of long bones. These are usually asymptomatic and found incidentally. The radiographic appearance is a classic plume of smoke rising up a chimney, representing a central lucency of normal marrow surrounded by sclerosis (Fig. 15.7). MRI distinguishes the contrast between normal marrow and surrounding sclerosis well. As bone infarcts are incidentally found, no treatment is indicated. However, the sclerosis may pose a physical challenge to the surgeon who is attempting to fix a fracture near this significantly harder bone.

Fig. 15.7 Bone infarct. Plain x-ray of bone infarct in the distal femur and proximal tibia. The plume of smoke in a chimney appearance is a classic descriptor

15.6 Pediatric Osteochondroses

Osteochondrosis is a focal aseptic necrosis in growing children and adolescents of physes undergoing endochondral ossification, the process in which cartilage is replaced by bone, and results in stunted growth that may fully recover or result in angular and length deformity. Osteochondrosis occurs at the epiphysis, the site of longitudinal growth, and at the apophysis, e.g., tibial tubercle, where bony prominences grow at the site of tendinous and ligamentous attachments in response to Wolff's law. The disease process is multifactorial and requires careful history and physical examination to distinguish it from other metabolic and inherited conditions [44, 45]. Osteochondrosis can occur along any epiphysis or apophysis in the body. However, if there is polyarticular involvement, then inherited physeal diseases including multiple epiphyseal dysplasia and spondyloepiphyseal dysplasia should be entertained [46]. The majority of osteochondrosis are classified by an eponym (Table 15.1).

15.6.1 Pathophysiology and Natural History

The pathophysiology of osteochondrosis is not well understood. Several theories have been postulated for development of ischemia including direct interference of the vascular supply and failure of bony enlargement resulting in disordered proliferation of cartilaginous cells. Inherited osteochondroses, thrombophilia, trauma, embolism, copper or zinc deficiency, infection, metabolic derangements such as seen in hypothyroidism or electrolyte deficiency, sickle cell anemia, and lysosomal storage disorders have all been implicated [45].

Table 15.1 Eponyms of osteochondrosis. The more common presentations are italicized. The table is divided into primary and secondary ossification centers representing the ossification center present at birth and the ossification center that develops later, respectively

Ossification center	Location	Eponym
Primary	Scaphoid	Preiser disease
	Lunate	*Kienböck disease*
	Medial cuneiform	Buschke disease
	Patella	Köhler disease
	Talus	Mouchet disease
	Navicular	*Köhler disease*
	Vertebral body	Calvé disease
Secondary	*Vertebral epiphysis*	*Scheuermann disease*
	Iliac crest	Buchman disease
	Symphysis pubis	Pierson disease
	Ischiopubic junction	Van Neck disease
	Ischial tuberosity	Valtancoli disease
	Calcaneal apophysis	*Sever disease*
	Accessory tarsal navicular	*Haglund disease*
	Second metatarsal	Freiberg disease
	Fifth metatarsal base	Iselin disease
	Talus	Diaz disease
	Distal tibial epiphysis	Lewin disease
	Proximal tibial epiphysis	*Blount's disease*
	Tuberosity of the tibia	*Osgood-Schlatter disease*
	Secondary patellar center	*Sinding-Larsen-Johansson syndrome (jumper's knee)*
	Lesser trochanter of the femur	Monde-Felix disease
	Greater trochanter of the femur	Mandl or Buchman disease
	Femoral capital epiphysis	*Legg-Calve-Perthes disease*
	Phalanges	Thiemann syndrome
	Metacarpal heads	Mauclaire disease
	Proximal epiphysis of the radius	Schaefer disease
	Distal epiphysis of the ulna	Burns disease
	Medial humeral condyle	Froelich disease
	Lateral humeral condyle	Froelich disease
	Humeral capitellum	*Panner disease (little league elbow)*
	Humeral head	Hass disease
	Clavicle	Friedrich disease

15.6.2 Diagnosis of Osteochondrosis

Diagnosis of osteochondrosis requires a careful history and physical examination. The presenting symptoms are often tenderness, loss of the normal arc of range of motion, edema, and effusion. Refusal to bear weight may occur and is often reported by the parent or caregiver. When osteochondrosis is being considered, radiographs of the affected extremity and adjacent articulations, electrolyte panel, complete blood count, and infection markers including ESR and CRP should be obtained [47]. Referral to a geneticist may be considered when additional skeletal and extraskeletal manifestations are present [46].

15.6.3 Imaging Findings in Osteochondrosis

X-ray The ossification center is often seen with a reduced size and irregular architecture with corresponding trabecular asymmetry (Fig. 15.8).

Fig. 15.8 Legg-Calvé-Perthes disease. Plain AP x-ray of a skeletally immature pelvis. The left proximal femoral ossification center is reduced in size and irregular compared to the normal appearance on the right

As the bone revascularizes and initiates healing, osteoporosis, absorption of necrotic tissue, and deformation of the diseased physis may be seen. Restoration of the normal bony architecture is common; however, incomplete healing may result in chronic deformity [47].

MRI Just like in AVN, MRI may aid in the diagnosis before plain radiographic changes are present. Early in the disease process, MRI may show focal hyperintensities in the epiphysis/apophysis or adjacent soft tissues. Marrow edema may also be apparent. The ossific nucleus may show irregularities. Revascularization and healing lead to replacement of the necrotic area with normal tissues [48].

Scintigraphy Scintigraphy is useful in detecting avascular regions and revascularization early in stages and is useful for tracking the progression from ischemia to necrosis to revascularization. Scintigraphy may show significant decrease in radiotracer uptake with ischemia, absent radiotracer uptake in necrosis, and increased radiotracer uptake with revascularization [49].

15.6.4 Treatment of Osteochondrosis

Although osteochondrosis causes fragmentation and collapse of the physis, it is self-limiting, the physis typically recovers, and growth resumes. However, failure to heal the physis completely or symmetrically can result in chronic pain and disability [44]. For example, Legg-Calvé-Perthes disease may cause proximal femoral shortening and coxa vara, Scheuermann disease may cause excessive kyphosis, and Blount's disease may cause tibial shortening and tibia vara. Just like other deforming diseases, the goal of treatment is to recreate length, rotation, and alignment and a congruent, mobile, and painless joint. Nonoperative modalities including braces, casts, physical therapy, and protected weight bearing may be used to support and guide the osteochondrosis while it heals. Surgery is indicated for those with resultant deformity or those expected to progress to deformity despite nonoperative modalities. Surgical options include osteotomy, limb lengthening, selective physeal arrest to reduce angular deformity, and contralateral physeal arrest to maintain limb length equality [45, 47].

15.7 Coagulopathic Disorders of the Musculoskeletal System

15.7.1 Hemophilic Arthropathy

Hemophilic arthropathy is a condition characterized by repetitive hemarthrosis and joint deformation, afflicting those with coagulopathic disease, commonly hemophilia. The knee is the most common afflicted joint followed by the elbow, ankle, shoulder, and spine. Patients with hemophilic arthropathy present with recurrent painful hemarthrosis causing limited range of motion with ensuing contracture formation and arthrosis [50]. Joint bleeding from microtrauma induces synovial hypertrophy and angiogenesis increasing vulnerability to further trauma and hemarthrosis. Cytokines and metalloproteinases present in the blood damage the articular cartilage resulting in an erosive arthropathy [51] (Fig. 15.9).

The diagnosis of hemophilic arthropathy involves radiographic imaging of the affected joint, arthrocentesis, and laboratory assessment.

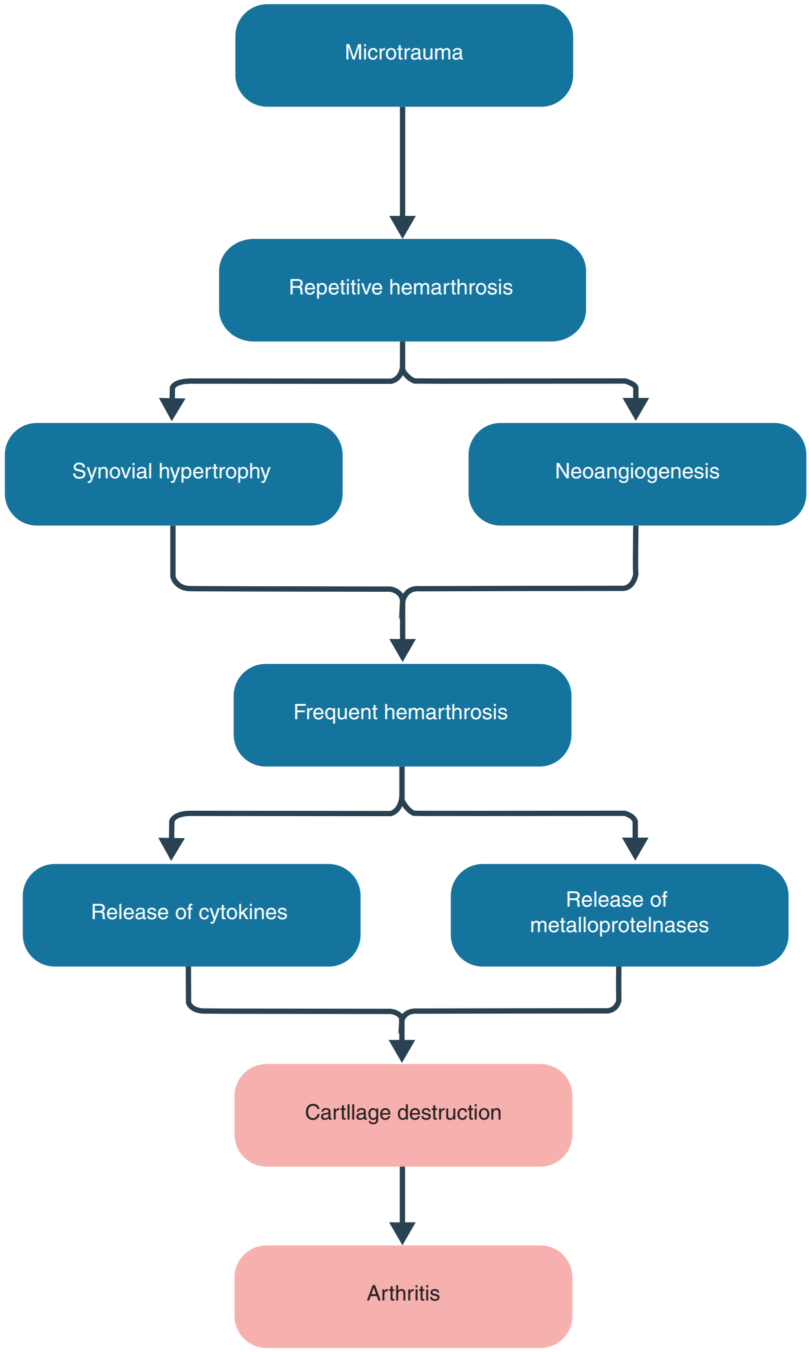

Fig. 15.9 Flow diagram of the pathogenesis of hemophilic arthropathy. Repetitive microtrauma results in hemarthrosis with synovial hypertrophy and angiogenesis. With frequent hemarthrosis, cytokines and metalloproteinases are released, resulting in cartilage destruction and arthritis

Radiographs classically appear initially with soft tissue edema, followed by generalized osteopenia, subchondral cysts, cartilage loss with joint space narrowing, and severe arthritic changes [50] (Fig. 15.10). Arthrocentesis is indicated to rule out other causes of inflammatory arthritides, including septic arthritis and crystalline arthropathy. Laboratory assessments of coagulation factors and hemoglobin level are mandatory, as hemarthrosis portends a higher chance of bleeding into catastrophic areas such as the epidural space or gastrointestinal tract.

Fig. 15.10 Plain x-ray of a left ankle with hemophilic arthropathy. There is significant erosive change in the tibiotalar joint, with joint space narrowing and periarticular osteopenia

Treatment is initially directed at symptomatic control with compressive dressing, analgesia, protected weight bearing, immobilization, and a rehabilitation protocol. Intraarticular steroids can help reduce inflammation and pain. Once nonoperative modalities have been exhausted, then synovectomy (surgical or radiation synovectomy), total joint arthroplasty, or arthrodesis is indicated [52, 53]. A hematologist should be consulted for factor repletion and reversal of anticoagulation prior to any operation [54].

15.7.2 Soft Tissue Hematoma

Coagulopathy increases the risk of spontaneous and post-traumatic soft tissue hematoma. While the majority of intramuscular hematoma can be treated nonoperatively with compressive dressing and repletion of factor levels or reversal of anticoagulants, hematomas that compress neurologic structures, such as spinal epidural hematomas, must be surgically decompressed to prevent permanent neurologic deficit. Intramuscular hematomas present with localized pain, erythema, and a fluctuant mass. Ultrasound, MRI, or CT may be used to confirm the diagnosis. Inflammatory markers including ESR, CRP, and WBC count should be obtained to rule out infection. Spinal epidural hematomas present with pain, erythema, and neurologic compromise. MRI is best used to confirm the diagnosis and evaluate for spinal cord compression. The most common cause of spinal epidural hematoma is postoperative. Idiopathic causes are rare [55].

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Bone Tumors

16

James Pascal Norris IV

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the clinical and radiographic features of bone tumors.
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Common presentation of bone tumors and the warning signs that suggest a malignancy
  2. Imaging modalities and characteristics of bone tumors
  3. General treatment strategies of bone tumors
  4. Basic characteristics and biologic behavior of the more common bone tumors seen in clinical practice

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16.1 Clinical Presentation

The goal of any thoughtful clinician should be to generate a focused differential from the patient's history, examination, and radiologic data, even before a tissue diagnosis is made. This helps focus further investigation and informs discussions with patients. Something as simple as age can help quickly narrow the differential [1]. For instance, a child with an aggressive bone lesion is much more likely to have a primary bone sarcoma than metastatic disease, while the opposite is true for an adult over 50. A primary bone sarcoma may be possible, but a metastatic or hematopoietic malignancy is overwhelmingly more likely.

Pain is a common presenting complaint for many musculoskeletal disorders, and the same is true for bone lesions. 71% of patients with bone sarcomas complain of deep pain at their initial presentation. Night pain is a classic warning sign of a bone sarcoma, but less than half of patients present with this complaint [2]. In general, pain is a fairly sensitive indicator of a bone sarcoma over a non-malignant etiology, with a sensitivity of 82% [3]. Remember, however, that benign etiologies will also present with pain [3].

Other symptoms include mass, swelling, and a limp [2, 3]. The combination of deep pain and a palpable mass is highly suggestive of a bone sarcoma with a specificity of 96% [3]. Distracting history items are common as well, with many patients (21%) reporting a history of trauma [2]. This issue further highlights the importance of a good differential and appropriate assimilation of available information.

16.2 Radiologic Findings

Numerous imaging modalities exist to help further the diagnosis, but this chapter will focus on the most common modalities, including conventional radiography, computed tomography, magnetic resonance imaging, technetium-99 bone scintigraphy, and positron emission tomography.

16.2.1 Conventional Radiography (XR)

Dr. William Enneking's eponymous four questions provide a helpful framework to interpret XR images in the setting of bony lesions: Where is the lesion located? What, if any, matrix is it producing? What is the lesion doing to the bone? What is the bone doing to the lesion?

Location refers to the three main areas of a long bone, namely, the epiphysis, metaphysis, and diaphysis (Fig. 16.1). Even from this seemingly simple question, a differential begins to take shape. A bone lesion in the epiphysis of a growing child can be one of only a handful of entities [1, 4].

The pattern of calcification of a lesion is the next thing to consider when interpreting radiographs. The calcification pattern speaks to the internal matrix of the lesion, either osseous, chondroid, or fibrous. Other lesions that lack a calcifying matrix will appear as purely lytic [1, 4, 5]. Descriptive terms are in the eye of the viewer, but common terms have persisted to describe the various matrices. Osseous calcifications are described as cloudlike, fluffy, or mottled. Chondroid calcifications are described as rings and arcs, flocculent, stippled, or popcorn. Finally, fibrous calcifications are described as smudgy or ground glass (Fig. 16.2). These calcifications mark another step along the diagnostic pathway, as an osseous lesion would not be expected to have a fibrous matrix and vice versa.

Next, the interaction of the bone to the tumor can be a vital indication of the aggressiveness of a given lesion. Bone will typically respond to a growing lesion by laying down new bone as its outer membrane, the periosteum, is perturbed or elevated by the mass. This periosteal reaction comes in several radiographic forms. More aggressive versions include onion skinning, Codman's triangles, and sunburst patterns. Onion skinning describes sequential layers of reactive bone laid down in response to an expansile lesion. Codman's triangles are similar, but suggest that the mass is eroding the layers faster than they can mature and only the peripheral portions of this

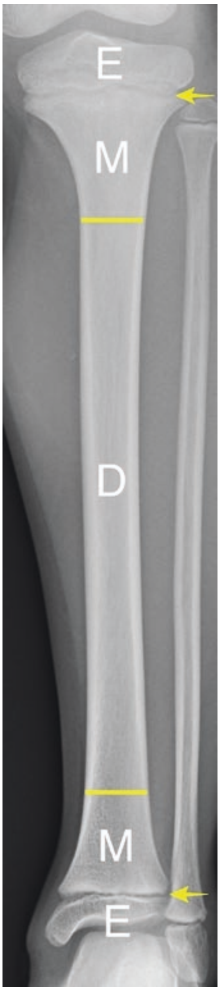

Fig. 16.1 Long bone regions. Note the three regions of a long bone, in this case the tibia, which can be used to describe bone lesions and narrow the differential. The epiphysis (E) is the bone between the physis and the joint surface. The metaphysis (M) is the widening area of bone between the tubular diaphysis and physis. The diaphysis (D) is the narrow, tubular portion with the thickest cortex. The physis (P) is the radiolucent area where longitudinal growth occurs via endochondral ossification

periosteal reaction persist. The spiculated, radially oriented, sunburst pattern is yet another form that suggests an aggressive process. A slow growing lesion will allow the bone to contain it, causing a periosteal reaction seen as cortical thickening or expansion [1]. This again helps narrow the differential. A benign lesion would not show the rapid growth necessary to create more aggressive periosteal reaction.

Finally, the interaction of the tumor to the bone can be another indication of the pattern and speed of growth and thus aggressiveness. Faster growing, more aggressive lesions erode the trabeculae and cortex. This is seen as purely lytic or lucent areas in the bone (Fig. 16.3). Further, they can also permeate the marrow spaces, causing a so-called "non-geographic" transition from lesion to healthy bone on XR. Put simply, it becomes difficult to define where the lesion stops and normal bone starts. In contrast, more indolent lesions, such as a UBC, will often have a sharp, potentially sclerotic border marking a clear, "geographic" distinction between lesion and bone (Fig. 16.4) [1, 4].

While the above presents a general framework, the radiographic appearance of similar lesions can vary widely [5]. This underscores the importance of gathering all the appropriate data from the history, radiology, and pathology.

16.2.2 Magnetic Resonance Imaging (MRI)

MRI is a key diagnostic tool in determining the characteristics of a lesion as well as its bony and soft tissue extent. The physics of MRIs are outside the scope of this chapter, but, briefly, it relies on the interactions of an induced magnetic field and the protons within the various tissues being imaged. Myriad sequences and techniques exist, but the three most important sequences for the imaging of bone tumors are T1, T2, and contrasted images.

On T1 imaging, fat is bright and water is dark. The distinction between tissues is the sharpest on T1 and is key to determining tumor extent and surrounding anatomy [4, 5]. For T2 sequences, the opposite is true—fat is dark and water is bright. Water is a sign of edema and is abnormally present in bony lesions of all types as well as in normal bone that is responding to a nearby active lesion. While anatomy is less distinct, areas of high T2 signal can highlight pathology more starkly [4]. Short tau inversion recovery (STIR) sequences are a similar fluid-sensitive sequence with even less anatomic detail but more

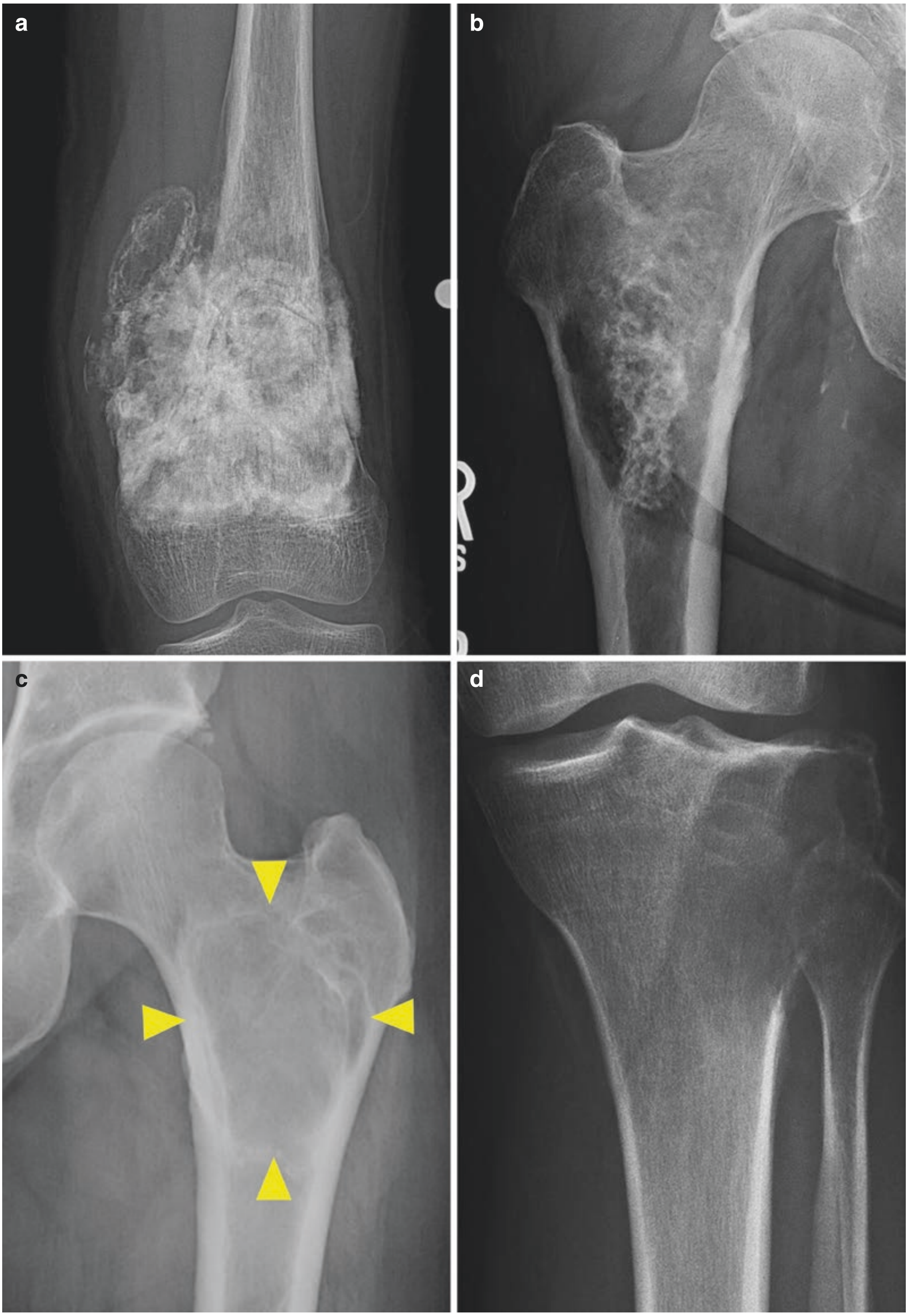

Fig. 16.2 Matrix calcifications. Image (**a**) demonstrates the fluffy, cloudlike densities consistent with osteoid matrix calcification in a patient with an osteosarcoma. Image (**b**) shows the stippled calcifications of chondroid matrix calcifications in a patient with a chondrosarcoma. Image (**c**) shows the smudgy, frosted glass pattern of fibrous matrix calcifications in a patient with fibrous dysplasia (yellow areas). Often subtle but is best compared to the nearby, normal, criss-crossing trabecular of the femoral head and neck. Finally, Image (**d**) shows the lucent lack of calcifications in a purely lytic lesion in a patient with a giant cell tumor of bone

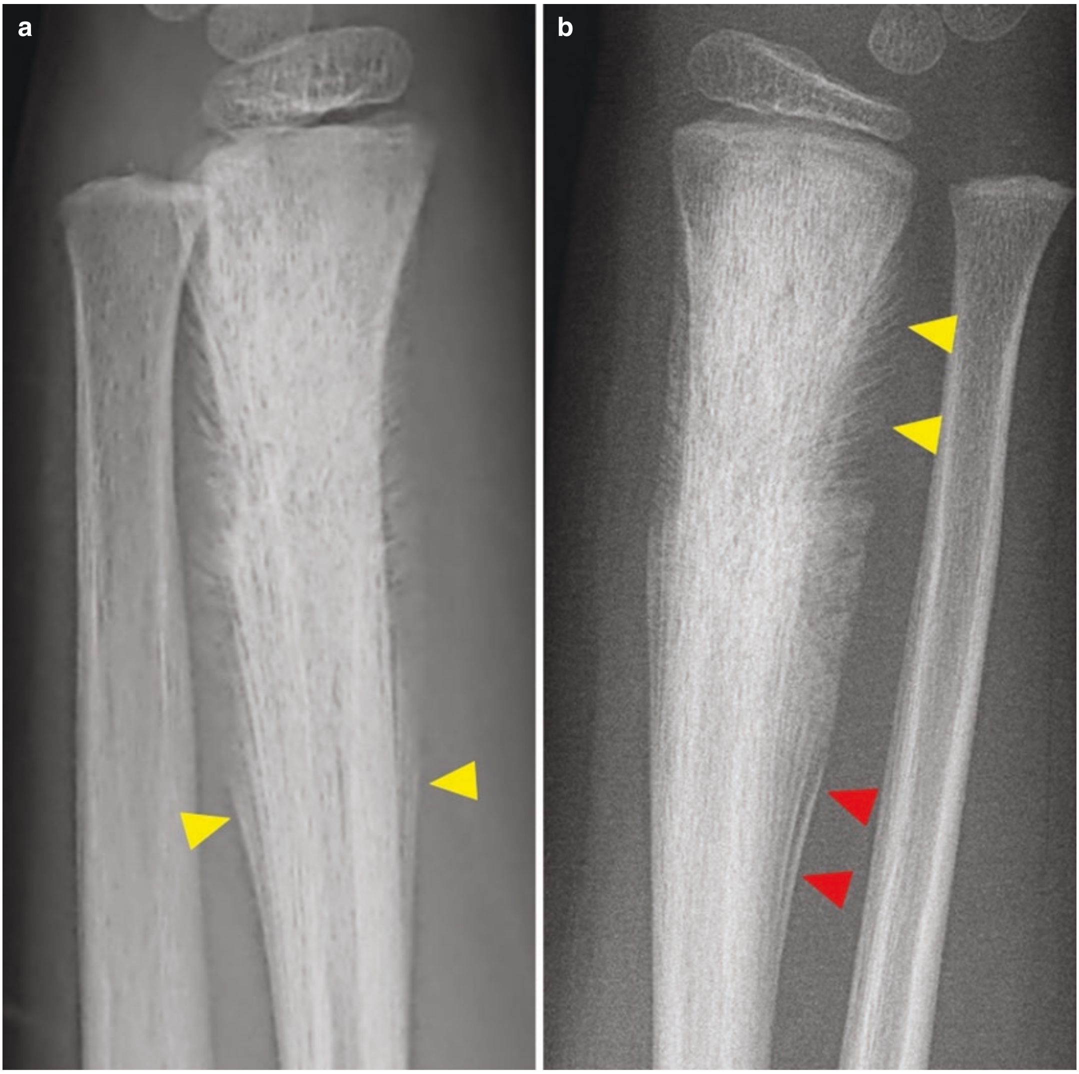

Fig. 16.3 Periosteal reaction. Images (**a**) and (**b**) are the orthogonal views of a patient with a distal radius Ewing's sarcoma. Image (**a**) shows Codman's triangles arising from the diaphysis proximal to the mass. Image (**b**) shows the layers, onion-skinning pattern proximally (red arrows) and the spiculated sunburst pattern distally (yellow arrows)

stark contrast between fluid and non-fluid areas. Finally, gadolinium contrast is taken up by biologically active tissue such as a growing tumor (Fig. 16.5). Cysts are a good example of how contrast can be helpful in comparison to basic T1 and T2 sequences [6]. On T2, a fluid-filled cyst will be uniformly high signal. Since the lining of a cyst is its only biologically active tissue, addition of contrast will show "rim enhancement" of the cyst, while the center will be unchanged. In contrast, a sarcoma will show high signal on T2 like a cyst, but as the more solid, biologically active lesion, it will show diffuse enhancement throughout.

While MRI is an excellent anatomic study and is very helpful at highlighting areas of pathology, it is rarely sufficient to make a specific diagnosis. Most malignancies will show aggressive features, but numerous benign entities will also appear quite concerning on MRI such as a

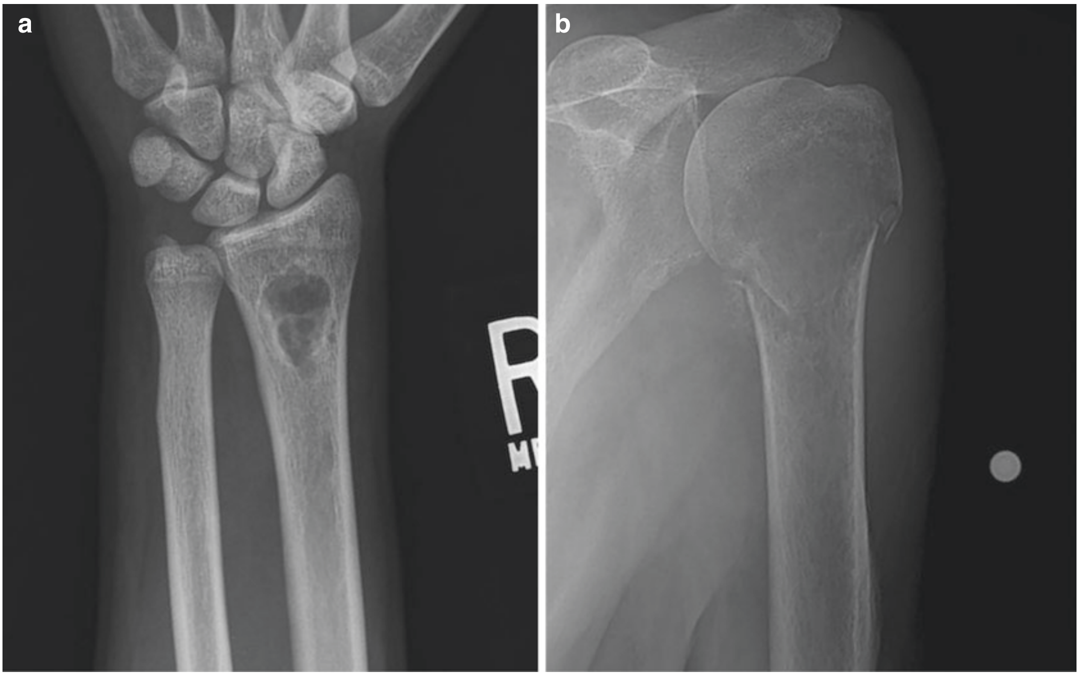

Fig. 16.4 Lesion borders. Image (**a**) shows the sharply demarcated, sclerotic border of a benign fibrous lesion in the distal radius. This "geographic" border sharply defines the lesions from the surrounding, normal-appearing bone. In contrast, Image (**b**) shows the poorly demarcated, permeative pattern of a metastatic lung cancer lesion in the proximal humerus. This "non-geographic" border makes it difficult to determine where the lesion stops and normal bone starts. A pathologic fracture is also present

chondroblastoma. Again, the MRI data must be incorporated to the larger clinical picture.

16.2.3 Computed Tomography (CT)

CT imaging has a number of advantages in the workup of bony lesions. As a synthesized "stack" of radiographs, it provides excellent information regarding bony anatomy. This can be helpful to determine subtle changes to the bony architecture and to assess bony stability. In limited cases, such as osteoid osteoma or myositis ossificans, the information can be sufficient for diagnosis [6]. CT angiography can be helpful to determine vascular compromise from a nearby lesion. In certain cases, a CT may be the only cross-sectional imaging option in patients with MRI-incompatible devices, such as pacemakers or cochlear implants. Finally, CTs are a key staging study. Chest CTs evaluate for lung metastases in the setting of a bone sarcoma, while CTs of the chest, abdomen, and pelvis evaluate for primary malignancies in the setting of bony metastases. While these studies provide complementary information, CTs have less soft tissue detail and do not highlight marrow changes as do MRIs.

16.2.4 Bone Scintigraphy

Bone scintigraphy (bone scan) is obtained by administering technetium 99m, a radiotracer absorbed by areas of osteoblastic activity in bone [7]. It relies on the body's response to a pathologic process rather than the pathology itself. Therefore, it is a very nonspecific test, as numerous conditions show abnormal uptake including sarcoma, metastatic disease, hematologic malignancy, fracture, infection, and benign entities [4]. Further, certain malignancies do not show uptake on bone scan, notably multiple

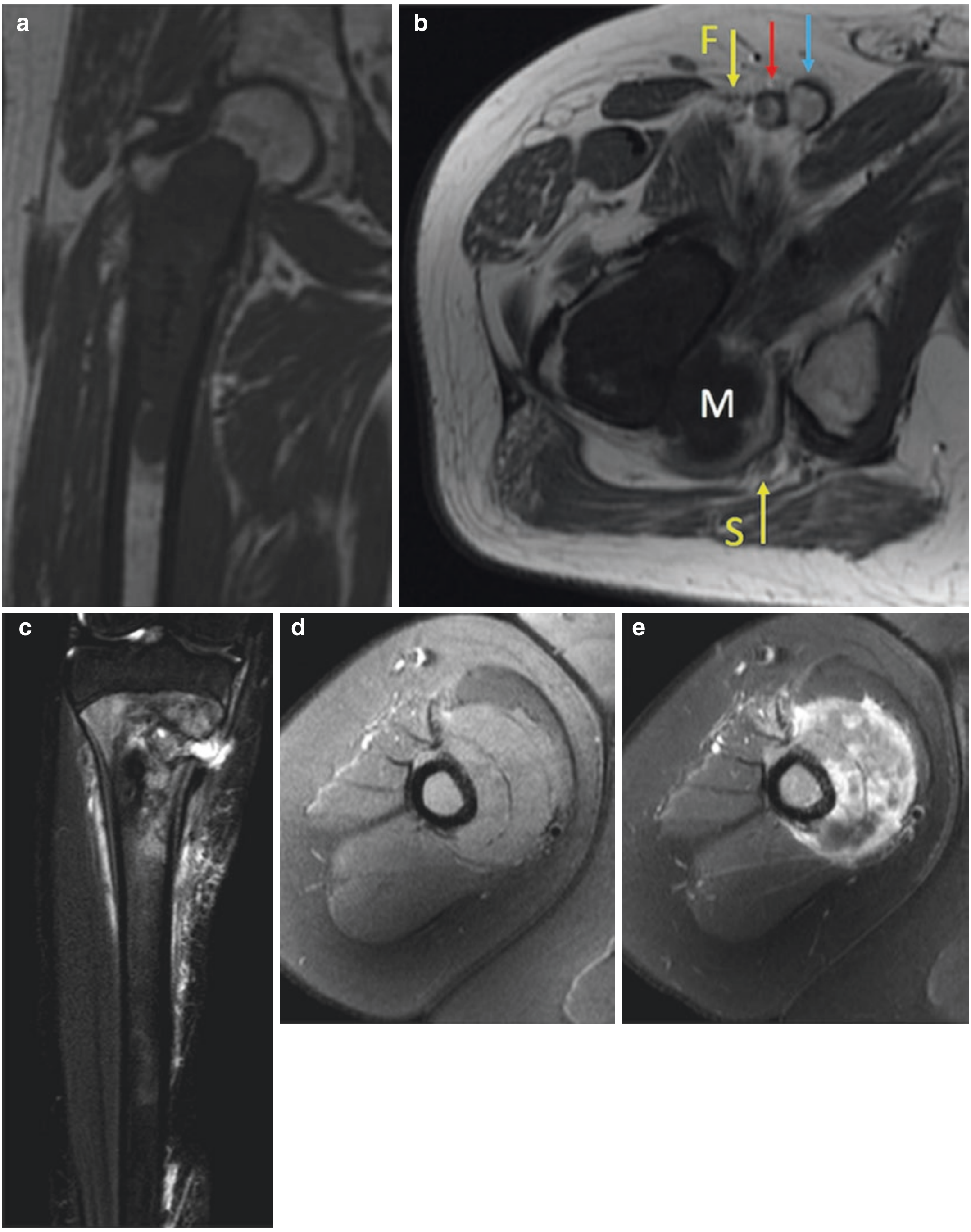

Fig. 16.5 MRI findings. Images (**a**) and (**b**) are the T1 coronal (A) and T1 axial (B) sequences in a patient with a proximal femur chondrosarcoma that highlights its use for anatomy and surgical planning. Image (**a**) shows the sharp demarcation between the normal, bright marrow fat and the dark, marrow-replacing mass. Image (**b**) shows the large posterior soft tissue mass (M) and its relation to the sciatic nerve (yellow arrow, “S”). The femoral nerve (yellow arrow, “F”), artery (red arrow), and vein (blue arrow) can be seen in the anterior aspect of the thigh. Image (**c**) is the coronal STIR sequence in a patient with a tibial Ewing’s sarcoma. Coronal, fluid-sensitive sequences (T2, STIR) can be helpful to quickly gauge the area of pathology. Images (**d**) and (**e**) are the precontrast (D) and postcontrast (E) T1, fat-saturated images of a patient with a proximal humeral Ewing’s sarcoma and a large soft tissue mass. This highlights the usefulness of contrast in further delineating the areas of pathology

myeloma. As such, bone scans are typically used to assess for other sites of disease when the underlying diagnosis has already been made as in polyostotic fibrous dysplasia, bone sarcoma, or metastatic carcinoma [4, 6–9]. They do not provide information regarding soft tissue masses nor those located solely in the marrow space [6].

16.2.5 Positron Emission Tomography (PET)

PET scans rely on a similar principle as bone scans, but they use a radioactive glucose molecule, ^{18}F-fluorodeoxyglucose (FDG), which is taken up by any metabolically active tissue. Thus, extraskeletal sites of disease can be seen [6, 8, 9]. The disadvantage is radiation exposure, as it is typically overlaid on a contemporaneous CT scan. Further, lesions must be a certain size to register abnormal activity, which may hinder detection of subtle, new findings like small lung nodules. PET scans have a high sensitivity for osseous bone sarcoma metastases, which increases the false positive rate, while bone scans have a higher specificity [8, 9].

16.3 Biopsy

Tissue analysis is the gold standard by which a definitive diagnosis is made, whether benign or malignant. In general, four methods of obtaining a biopsy exist. From least to most invasive, they are fine needle aspiration (FNA), core needle biopsy, open biopsy, and excisional biopsy. Fine needle aspirations are often not possible for bony lesions unless a large and easily palpable soft tissue mass is present. While quick and easy to obtain, the aspiration destroys the structural anatomy of the specimen, allowing for an analysis of only the cells. Core biopsy involves a much larger needle that has the ability to take a long, narrow "core" of tissue. This preserves the architecture and improves diagnostic accuracy. Open biopsy is obtained through a small, well-planned incision and allows for a larger sample of tissue. While potentially more accurate, open biopsies risk seeding the exposed tissue with cells from the violated tumor. It is common practice to excise the open biopsy tract at the time of definitive resection if a primary bone malignancy is confirmed. Further, poorly planned biopsies can lead to wound complications, suboptimal resections, and amputations [10].

It is appropriate to start with a core needle biopsy, with or without image guidance as dictated by the size, depth, and location of the mass. These have been found to be 80–95% accurate [11–13]. Thus, there is an 80–95% chance that a diagnosis can be made with a less invasive, less expensive, lower-risk procedure, obviating the need for open biopsy [10, 13]. An open procedure can be reserved for non-diagnostic or challenging core specimens when a larger sample could help clarify the diagnosis.

16.4 Histology

An in-depth examination of musculoskeletal pathology and histology is outside the scope of this chapter. However, in general the goal of the histology is to make a definitive diagnosis. Unlike soft tissue sarcomas, where the grade of histology correlates to clinical aggressiveness, the character of bone lesions is typically set by the diagnosis. For instance, Ewing's sarcoma is by definition a high-grade lesion, whereas a parosteal osteosarcoma is generally low grade. Characteristic findings will be discussed later in this chapter, but in general, malignancy and clinical aggression are suggested by several histologic findings, including cellular pleomorphism (cells of varying shapes and sizes), nuclear atypia (nuclei of varying shapes, sizes, and densities), increased mitotic figures, and necrosis (areas of dead tissue) [14]. Cellular morphology can suggest a tissue of origin. Sarcomas commonly—but not universally—are composed of spindle cells, i.e., long, thin cells with elongated nuclei consistent with their mesenchymal origin. Epithelioid cells, commonly seen in metastatic lesions, are rounded and can arrange in glands consistent with their origin in skin and viscera. Hematopoietic malignancies will have morphol-

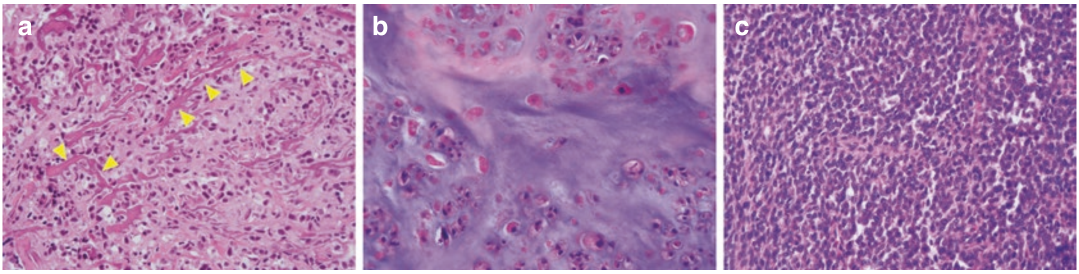

Fig. 16.6 Classic bone sarcoma pathologic findings. Image (**a**) is a high-power image from a high-grade, conventional osteosarcoma. Note the pleomorphic cells and lacey, pink, immature osteoid (yellow arrows). Image (**b**) shows the dense, purple chondroid matrix of a chondrosarcoma. This matrix would look similar in other chondroid lesions, but the number of cells and their specific morphology in this specimen makes the diagnosis of a chondrosarcoma. Image (**c**) shows a Ewing's sarcoma and the sheets of so-called small round blue cells classic to this lesion. Several other entities have a similar general appearance; thus, other staining and molecular tests are needed to determine the exact diagnosis

ogy similar to various cell lines seen in bone marrow, such as T or B cells, suggestive of lymphoma, myeloma, or leukemia. Matrix production can also give a clue to the cell of origin or diagnosis, such as osteoid or chondroid (Fig. 16.6). Once obtained, immunohistochemistry stains are used to further narrow the differential. Finally, genetic testing like fluorescent in situ hybridization (FISH) and PCR can be used to determine characteristic mutations and markers, such as the EWS gene mutation of Ewing's sarcoma.

16.5 Treatment Strategy

16.5.1 Observation

The most basic—and most important—decision for a surgeon is when to operate. Many asymptomatic bone tumors will be diagnosed incidentally during the workup of other complaints. Tibial non-ossifying fibromas (NOFs) can be seen on X-rays obtained after an ankle sprain. Enchondromas of the humerus can be seen on chest XR obtained for pulmonary complaints. It would be inappropriate to operate on these asymptomatic, benign lesions.

When a quiescent lesion is suspected and all clinical signs point to another cause of a patient's symptoms, observation is an appropriate strategy. Active surveillance is a more appropriate term, as it is important to obtain serial images to confirm stability of a presumed benign lesion. No history or exam findings are iron clad in determining a diagnosis; thus, time can be a key diagnostic tool. A rotator cuff tear is reasonably expected in an older patient with overhead pain, characteristic evocative testing, and relief with a local injection. However, enlargement of a proximal humeral chondroid lesion on serial imaging in the same patient would favor a chondrosarcoma regardless of the presence or absence of rotator cuff pathology.

The interval of observation must be guided by the clinician's relative confidence in the presumed diagnosis. Higher clinical suspicion would warrant follow-up imaging in 4–6 weeks, while low concern would dictate an interval of 4–6 months.

16.5.2 Percutaneous Intervention

The next more invasive treatment along the spectrum is percutaneous therapy. Numerous forms exist, but in general they are utilized for focal, benign lesions when a reasonable chance of healing is expected. The classic example is radiofrequency ablation (RFA) for an osteoid osteoma. As discussed later in this chapter, osteoid osteomas have a small, central nidus surrounded by dense reactive bone. The nidus itself is the neoplastic portion of the lesion, which can be easily treated by RFA while offering minimal risk as the

surrounding bone acts as a shield for the surrounding tissue. Previously, the area of bone would have been removed en bloc, but RFA offers a less invasive and equally—if not more—effective treatment strategy [15]. Numerous other examples exist, including steroid injections or cannulated screw placement for UBCs, doxycycline injections for ABCs, and RFA of bony metastatic disease [16–19]. Percutaneous treatments are reasonably chosen even if not quite as effective because they can still offer the opportunity to avoid surgery while exposing patients to a lower risk of complications. Surgical intervention can always follow an unsuccessful percutaneous treatment without significant interference from the prior treatment.

16.5.3 Surgical Treatment

16.5.3.1 Intralesional Resection

Intralesional resection involves opening the affected bone and removing the lesion from within and is chosen when margin status is not critical to treatment outcome. Recurrent or locally aggressive benign lesions, low-grade sarcomas, and metastatic disease can all be safely and effectively treated by this method. Manual curettage (scraping) of the contents of the mass is typically coupled with a local adjuvant treatment. High-speed burring of the lining of the cavity physically removes the remaining disease [20, 21]. Chemical treatments such as hydrogen peroxide, phenol, liquid nitrogen, and denatured alcohol kill the remaining cells [20, 22, 23]. Argon laser achieves a similar goal [24]. The heat generated from the exothermic hardening of bone cement may have a cytotoxic effect on residual cells [20, 22, 23]. There is no evidence that graft choice significantly affects the possibility of local recurrence, however.

Intralesional treatment will often leave the bone significantly weakened, requiring filling the void with bone cement or bone graft and/or augmenting stability with a plate, screws, or intramedullary nail (Fig. 16.7).

16.5.3.2 En Bloc Resection

En bloc resection involves removing the entire diseased bone, usually with a margin of healthy bone and soft tissue surrounding the specimen. This is warranted in high-grade bone sarcomas where even microscopic residual disease can lead to increased risk for recurrence [25]. In large metastatic or locally aggressive lesions, the bone may be unsalvageable via intralesional techniques and en bloc resection is warranted to restore function.

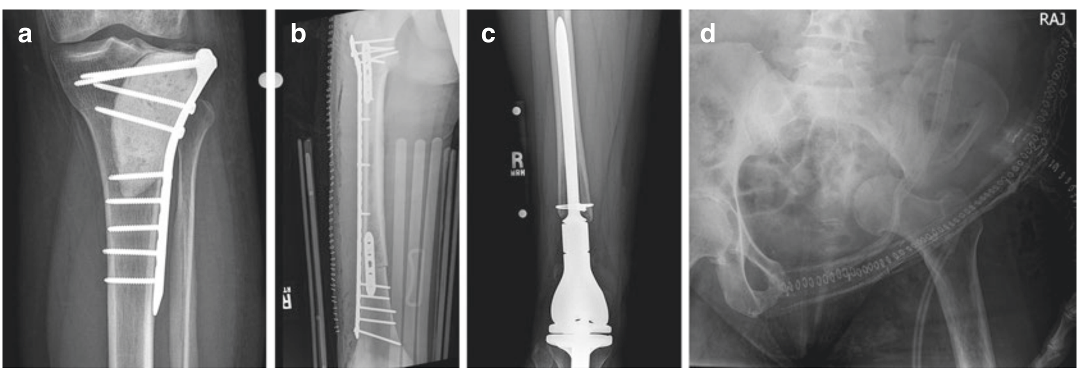

Fig. 16.7 Reconstruction after bone lesion resection. Image (**a**) shows cement and plate augmentation after intralesional resection of a proximal tibial giant cell tumor. Image (**b**) shows an intercalary allograft reconstruction after resection of a diaphyseal femoral Ewing's sarcoma. Image (**c**) shows an endoprosthetic reconstruction of the entire distal femur after en bloc resection for osteosarcoma. Image (**d**) shows an internal hemipelvectomy without reconstruction, i.e., a resection arthroplasty, in a patient with a post-radiation skeletal sarcoma. This may be warranted in patients who have a high risk for complications that would lead to removal of any attempted reconstruction implants

If limb salvage is to be completed, reconstruction must follow en bloc resection. This can come in the form of resection arthroplasty, intercalary or osteoarticular allograft, or endoprosthetic replacement (Fig. 16.7). Each of these options is accompanied by a set of relative risks and benefits. Resection arthroplasty, i.e., resection of one side of a joint without replacement, is technically easier, requires less operative time, and has no chance for hardware complications. However, it significantly alters the function of a limb and is often accompanied by lifelong discomfort [26, 27]. Allograft reconstruction offers a durable, biologic option that does not have to be revised but exposes patients to the risk of infection, nonunion, and allograft fracture [28]. Plus, patients are unable to bear weight for a prolonged period after surgery. Finally, endoprosthetic reconstruction offers immediate fixation and allows for early mobilization but has a higher risk of infection, dislocation, and shorter implant survival than traditional joint replacements, often requiring revision [29].

16.5.3.3 Amputation

Pioneering work in the 1970s and 1980s proved that limb salvage is a viable alternative to amputation in the setting of primary bone sarcomas. While a higher rate of local recurrence is seen, overall patient survival is equivalent between the two [30, 31]. Thus, the standard of care today is limb salvage. However, situations arise when extensive tumor involvement, persistent infection, and chronic pain limit the opportunity for or maintenance of limb salvage. In these settings, amputation is either the only reasonable option or the best available option for reliable restoration of function.

16.5.4 Adjuvant Treatment

In general, adjuvant, i.e., additional, treatment strategies that augment primary resection of the mass fall into two categories, systemic chemotherapy or local external beam radiation. With a few exceptions, systemic chemotherapy is used to treat disseminated disease. While it can have local therapy effect on the primary lesion, the goal is to treat distant disease or prevent its development. When the bone lesion is the distant disease, such as in the setting of metastatic carcinoma, chemotherapy is a mainstay of both local and systemic treatments. Chemotherapeutics come in numerous forms, including cytotoxic agents (vincristine, doxorubicin), immunologic agents (nivolumab), and targeted therapies (denosumab for giant cell tumor). They are often used in codified regimens such as MAP for osteosarcoma, VAC/IE for Ewing's sarcoma, or R-CHOP for lymphoma. The detriments of chemotherapy can be self-limiting like cytopenia, alopecia, nausea, and GI distress or more long standing like sterility, neuropathy, or cardiomyopathy. They also put patients at risk for hematologic malignancy.

Alternatively, radiation is used to treat local disease whether a primary bone sarcoma or metastatic disease. While used more commonly in soft tissue sarcomas, radiation can still be effective for certain primary bone lesions. Due to the particular sensitivity of Ewing's sarcoma, radiation can be used as a primary local control strategy for unresectable disease or to augment resection when negative margins cannot be obtained. For metastatic disease, radiation is used primarily to halt progression or postoperatively to treat remaining disease, progression of which leads to continued pain and threatens the survival of the reconstruction. While ionizing radiation kills cancer cells, its effects on healthy tissue are significant and include lymphedema, fibrosis, skin ulceration, and wound healing complications. The induction of DNA damage is typically cytotoxic, but it also exposes people to mutations that can progress to a post-radiation sarcoma, which occurs at a rate of 0.06% [32].

Not all bone lesions respond similarly to these treatments. Ewing's sarcoma is markedly sensitive to both modalities. Osteosarcoma is chemosensitive but relatively radiation resistant. Chondrosarcomas are notoriously refractory to both. The most important aspect of adjuvant therapy is the involvement of a multidisciplinary team to determine when and how to utilize these modalities.

16.6 Specific Diagnoses

16.6.1 Benign Bone Tumors

16.6.1.1 Unicameral Bone Cyst (UBC)

UBCs are simple, fluid-filled cysts characteristically found in the metaphysis of long bones in children. Radiographically, they will appear as lytic lesions with a sclerotic border and peripheral sclerotic ridges. They can thin and even expand the cortex but should not expand past the width of the nearby physis [33]. This is one of a handful of entities for which XRs can reliably make the diagnosis. The “fallen fragment” sign, a small cortical fragment at the inferior aspect of the cyst cavity on X-ray, is almost pathognomonic [34]. MRI will show a uniform, T2 hyperintense lesion with rim enhancement on postcontrast images (Fig. 16.8). The lesion itself is typically not painful, but can cause symptoms if it has thinned the bone enough to cause stress fracturing. Pathologic fracture is not an uncommon presentation but has a reasonable opportunity to heal (Fig. 16.8). Histologically, the lesion will have a thin, connective tissue lining with hemosiderin staining and occasional giant cells [33]. Numerous percutaneous treatments have been proposed, including steroid injection, cannulated screw placement, and injection of bone graft substitute [16, 17, 35]. Invasive treatment can be with curettage and bone grafting or cementing if symptoms continue despite percutaneous treatment. All offer a reasonable chance of resolution ranging between 77% and 98% [17].

16.6.1.2 Aneurysmal Bone Cyst (ABC)

Commonly found in children, ABCs are radiographically similar but pathologically and clinically distinct lesions from UBCs. Radiographically, they are lytic, metaphyseal lesions but will have more internal septations and can expand the cortex past the width of the physis. MRI will show a multi-loculated cyst often with fluid-fluid levels caused by layering of blood and fluid within the cyst. Histologically, fibrous septae with moderate cellularity with scattered intramural giant cells and “blood lakes” filling the cyst spaces will be seen [36]. Percutaneous therapy has been studied in the form of doxycycline injection and can halt progression and thicken the cortex [18]. Due to the associated pain and structural weakness, intralesional resection remains the mainstay of treatment [18]. The recurrence rate is relatively high, with curettage and high-speed burring offering a 3–20% chance of recurrence [21, 37]. Additional argon laser treatment to the cavity can decrease but not eradicate the risk for recurrence [37].

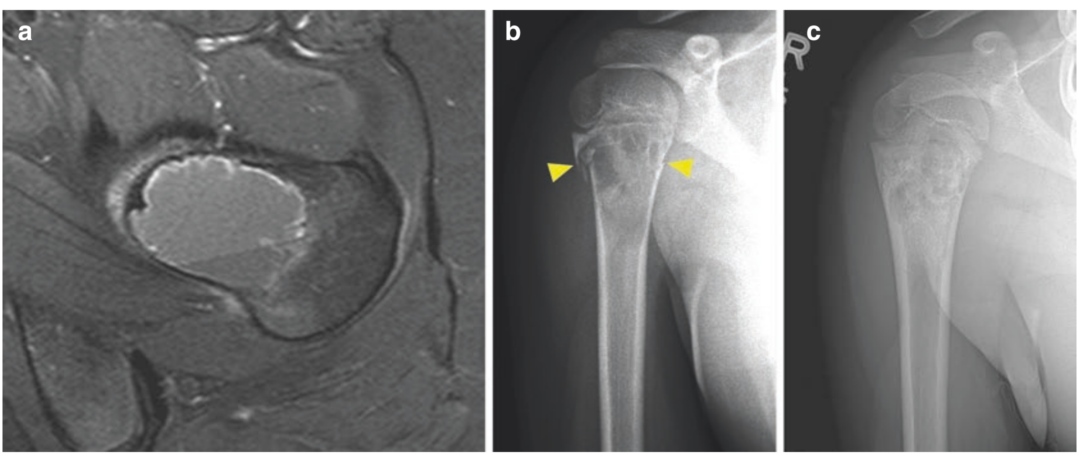

Fig. 16.8 Unicameral bone cyst. Image (**a**) shows the characteristic peripheral rim enhancement of a UBC of the proximal femur. A fluid-fluid level is present, which is a nonspecific finding that is more commonly associated with an aneurysmal bone cyst. Images (**b**) and (**c**) show a pathologic fracture (yellow arrows) through a proximal humerus UBC with subsequent healing several months later (C)

16.6.1.3 Osteoid Osteoma/Osteoblastoma

Osteoid osteomas and osteoblastomas are histologically similar lesions that exist on a spectrum of size and location. Osteoid osteomas commonly present with pain that is typically worse at night and is significantly relieved with anti-inflammatories [38, 39]. Radiographically, osteoid osteomas are cortically based and consist of a small (<2 cm), central nidus surrounded by dense bone. The surrounding bone can obscure the nidus on XR, making CT helpful for diagnosis [40, 41]. Osteoblastomas are larger (>2 cm) and lucent and have a thin rim of surrounding bone. Approximately one third will occur in the spine and sacrum [40, 42]. Histologically, the center of each lesion will show vascularized, fibrous stroma with immature woven bone surrounded by osteoblasts [39, 40, 43]. Due to the small, central nidus, osteoid osteomas can be treated with percutaneous radiofrequency ablation with a success rate of 91–95% [15, 44]. Due to the larger size, osteoblastomas typically require intralesional resection or en bloc resection, which offer a moderate chance of recurrence of 24% and 13%, respectively [42].

16.6.1.4 Osteochondroma

Osteochondromas are exophytic, cartilage, and bone-forming lesions that favor the metaphysis of long bones. They are usually painless but may cause symptoms if adequately large. Imaging will reveal a thin cartilage cap overlying a pedunculated or sessile bony prominence with peripheral cortication and central trabecular bone. The hallmark finding that distinguishes these from other surface lesions is confluence of the medullary canal with the trabeculae of the osteochondroma (Fig. 16.9). Histologically, the cartilage cap consists of disorganized hyaline cartilage, morphologically similar to that of the normal physis with associated endochondral ossification [45, 46]. They are covered by a thin, fibrous, "perichondrium" that is continuous with the surrounding periosteum. The cartilage cells will show mutations of EXT1 and/or EXT2 which cause uncontrolled proliferation of chondrocytes. Spontaneous mutations are seen in solitary lesions, whereas an autosomal dominant mutation can lead to the familial disorder multiple hereditary exostoses (MHE) marked by multifocal osteochondromas that often cause growth abnormalities [45]. If warranted, lesions are treated with resection of the exostosis and its cartilage cap. Malignant transformation to chondrosarcoma is possible and occurs at a rate of 2–8% of solitary lesions and 9–36% in MHE patients [46–48]. Transformation is suggested by pain, growth of the lesion after skeletal maturity, lucency within

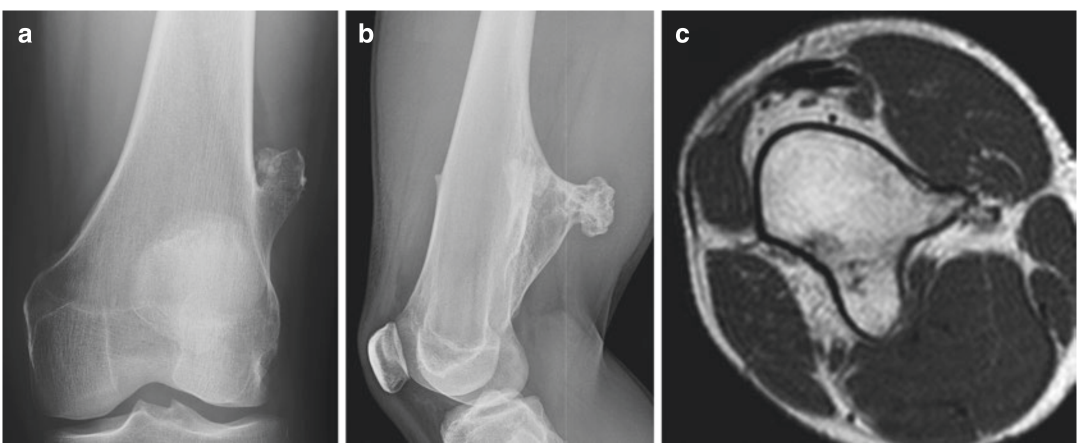

Fig. 16.9 Osteochondroma. Image (**a**) shows a classic pedunculated osteochondroma. Note that the medullary space is confluent with that of the mass. Image (**b**) shows an osteochondroma that is sessile, i.e., broad based, close to the femur with a smaller, pedunculated portion peripherally. The more irregular pattern is commonly seen in patients with multiple hereditary exostoses. Image (**c**) shows the MRI of the patient in image (**b**), further demonstrating the confluent marrow space between the osteochondroma and the underlying femur

the underlying bone, or a cartilage cap that is thicker than 2 cm on MRI [49].

16.6.1.5 Chondroblastoma

Chondroblastomas are one of few lesions that occur in the epiphysis of long bones in children and young adults [50, 51]. Pain is the most common presenting symptom [52]. Radiographically, they are marked by a well-defined, geographic lucency in the epiphysis. MRI will show exuberant bony edema surrounding a relatively small mass. Histology reveals sheets of homogenous, polygonal chondroblasts with scattered giant cells and areas of chicken wire calcifications—the pathognomonic finding (Fig. 16.10) [50, 51]. They are treated with intralesional resection with chemical and mechanical adjuvants and structural augmentation, but complete resection is limited by their location in the subchondral bone. Thus, the rate of recurrence is high, ranging between 5% and 40% [50, 52].

16.6.1.6 Enchondroma

Enchondromas are benign, cartilaginous proliferations often incidentally found in the metaphysis of long bones. XR will show a central lesion with stippled or popcorn-like calcifications (Fig. 16.11). Shallow scalloping of the cortex can be seen. Lesions of the extremities should be inactive and should not grow nor cause pain. Alternatively, lesions of the digits are lytic and expansile and can lead to pathologic fracture. Histologically, they are hypocellular lesions with abundant, pale blue chondroid matrix and peripheral calcifications. They can have binucleated chondrocytes or multicellular lacunae, making the pathologic distinction between enchondroma and low-grade chondrosarcoma very difficult [53]. The diagnosis of chondrosarcoma over enchondroma is a clinical and radiographic one and is based on pain, pathologic fracture, growth of the lesion, progressive lucency, or cortical erosion. Extremity lesions do not require treatment and can be followed radiographically. They have a 4–6% chance of progression to a chondrosarcoma [48, 54]. Lesions of the hands and feet may require intralesional treatment if symptomatic. Ollier's disease and Maffucci's syndrome are two hereditary conditions marked by multiple enchondromas. These disorders carry a risk for chondrosarcoma of 40% and require routine radiographic monitoring [55].

16.6.1.7 Non-ossifying Fibroma

Non-ossifying fibromas (NOFs) are eccentric, metaphyseal lesions mostly found in the long

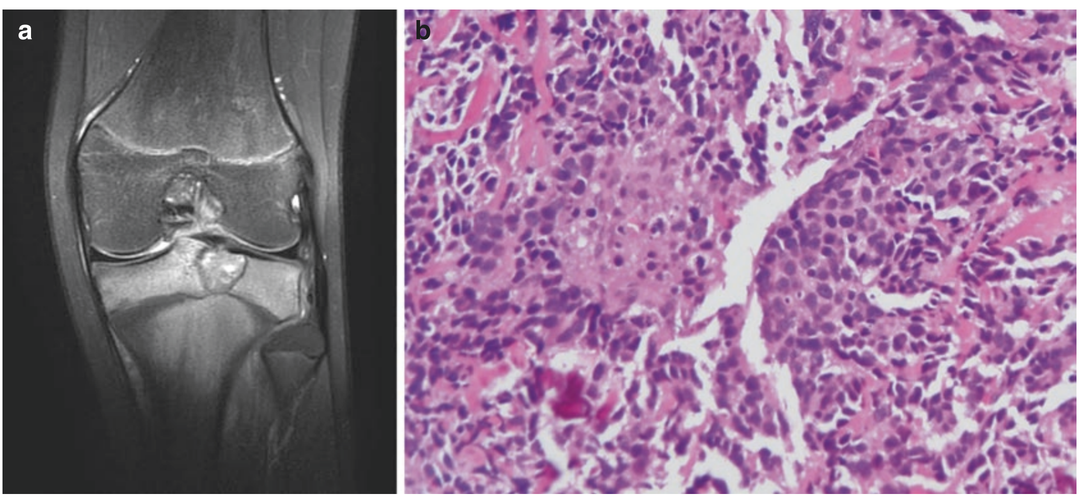

Fig. 16.10 Chondroblastoma. Image (**a**) shows the imaging hallmark of a small, epiphyseal lesion with diffuse and stark surrounding edema, here seen filling the entire epiphysis and the proximal metaphysis of the tibia. Image (**b**) is the pathology specimen of a chondroblastoma showing the uniform polygonal cells. In certain areas, not pictured here, dark, purple calcifications can be seen in between these cells forming the classic "chicken-wire" pattern

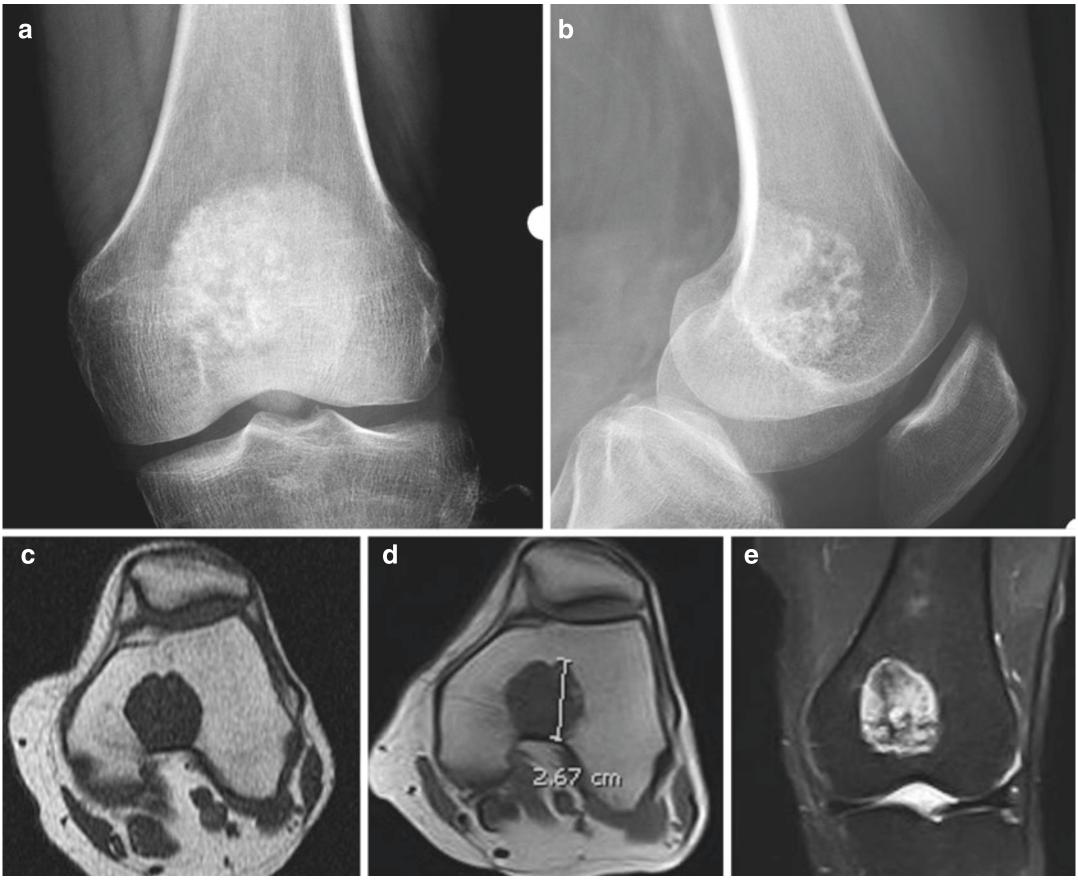

Fig. 16.11 Enchondroma. Images (**a**) and (**b**) are orthogonal views of an incidentally discovered distal femur osteochondroma in a patient with meniscal pathology. Images (**c**) and (**d**) show no change in size across serial MRIs. Image (**e**) shows no surrounding edema. All of which suggest a benign diagnosis

bones of the lower extremities. They are generally asymptomatic and are commonly found incidentally during the workup of unrelated complaints such as an ankle sprain or knee injury. XRs show a lytic, eccentric, metaphyseal lesion with sclerotic borders and "soap-bubble" septations (Fig. 16.12). As patients age, NOFs will typically ossify and become sclerotic. Histologically, they are composed of bland, homogenous, spindle-shaped fibroblasts arranged in a storiform, i.e., whirled or cartwheel, pattern [56, 57]. They generally do not require treatment. If the lesion is in its least calcified form and occupies the majority of the metaphysis, they can become symptomatic or lead to pathologic fracture which is managed with fixation and possible curettage if warranted (Fig. 16.12) [58].

16.6.1.8 Fibrous Dysplasia

Fibrous dysplasia is a fibrous proliferation in the medullary space most commonly of the femur, tibia, and craniofacial bones. Polyostotic forms exist in McCune-Albright syndrome, which is associated with endocrinopathies, and Mazabraud syndrome, which is accompanied by intramuscular myxomas. Symptoms vary widely from asymptomatic to chronically painful and deforming. XRs show cortical expansion and the characteristic "ground glass" calcifications. Constant microfracturing from structural weakness can cause significant remodeling and deformity, classically of the proximal femur. MRI is typically required to determine the intramedullary extent. Histology reveals a bland, hypocellular fibrous stroma

Fig. 16.12 Non-ossifying fibroma. Image (**a**) reveals a pathologic fracture through an NOF suffered during a football game. Note the classic, eccentric, geographic, soap-bubble lesion without surrounding lucency or periosteal reaction. Image (**b**) shows near-complete healing and consolidation of the previous NOF several months after plate and screw fixation

with islands of immature, irregularly shaped bone, described as "alphabet soup." Cystic, cartilaginous, and myxoid areas are not uncommon. While most isolated lesions will remain asymptomatic and ossify with age, symptomatic lesions or polyostotic disease can be treated with bisphosphonates [59, 60]. Intralesional resection is often ineffective so surgical treatment aims to maintain and/or restore stability and alignment with fixation and osteotomy, respectively [61].

16.6.2 Malignant Lesions

Due to the potential for metastases, malignant bone lesions require staging, i.e., a defined series of studies meant to identify all the sites of disease.

This section will identify the appropriate staging studies for each lesion.

16.6.2.1 Giant Cell Tumor of Bone

Giant cell tumor of bone (GCT) is a lytic epiphyseal and metaphyseal lesion that is locally aggressive with a low metastatic potential—approximately 4% [23, 62]. The low metastatic potential makes classification between benign and malignant difficult. This, along with chondroblastoma, is one of the few lesions that will occupy the epiphysis. The age of onset is slightly older, with peak incidence between 20 and 45. Pain is the main presenting complaint, with pathologic fracture possible. XR will show a purely lytic lesion with moderately geographic borders. A soft tissue mass is possible as these lesions can expand and erode the cortex; thus, MRI is helpful to evaluate the full extent of the lesion. Metastases occur in the lungs; thus, a CXR is required for staging. Microscopically, the lesions consist of uniform spindle to round mononuclear stromal cells with numerous, reactive multinucleated giant cells. The nuclei of the mononuclear cells are the same size as those in the giant cells [62]. Due to the high rate of recurrence, intralesional resection must be accompanied by local adjuvants for adequate resection, including high-speed burr, hydrogen peroxide, and argon laser. Structural support with cement and plate fixation is common as these lesions weaken the bone supporting the nearby joint [20, 22–24]. If subchondral bone destruction precludes bony preservation, en bloc resection and endoprosthetic replacement may be necessary. Unresectable lesions can be treated with denosumab, a monoclonal antibody that inhibits osteoclastic bone resorption [63].

16.6.2.2 Osteosarcoma

Osteosarcomas typically arise in the metaphysis of long bones and have a bimodal age distribution. The largest peak occurs between 10 and 14 years of age with a second, smaller peak over 60. The adult lesions often occur secondary to other processes, such as Paget's disease or bone infarct. Progressive, deep-seated pain and a mass are common. XRs will show a non-geographic lesion with areas of lucency mixed with osteoid matrix calcifications and aggressive periosteal reaction (Fig. 16.2, image a). Histology reveals markedly atypical and pleomorphic cells. The diagnosis hinges on the production of immature, "malignant" osteoid but chondroid and fibroblastic areas can be seen (Fig. 16.6). Several variants exist with varying aggressiveness, including chondroblastic, telangiectatic, parosteal, and periosteal [64].

Metastases occur most commonly in the lungs and bones, either within the affected bone—so called skip lesions—or in distant skeletal sites. Staging consists of an MRI of the entire affected bone to assess the extent of primary disease and rule out skip lesions, a whole-body bone scan to rule out distant skeletal metastases, and a chest CT to rule out lung metastases [65].

Treatment consists of preoperative chemotherapy in the form of MAP (methotrexate, Adriamycin, and cisplatin) followed by en bloc, wide resection with resumption of chemotherapy 10–14 days later. Higher local recurrence rates are seen with limb salvage, but overall survival is unchanged [31]. Local recurrence is affected by the presence of a positive surgical margin, defined as <1 mm of healthy tissue between the lesion and the edge of the specimen [25]. Non-metastatic, conventional osteosarcoma in children has 5- and 10-year overall survival rates of 69% and 59%, respectively [66] . Survival increases to over 80% with negative margins and over 90% microscopic tumor necrosis after preoperative chemotherapy [65, 67]. Survival is most significantly affected by the presence of metastases, which lowers the 5- and 10-year survival to 29% and 24%, respectively [68]. Survival is further limited by age >18 [66, 69], pelvic location [70, 71], less than 90% necrosis [65, 67], greater than 21 days to resumption of chemotherapy [72], and potentially pathologic fracture [73].

16.6.2.3 Ewing's Sarcoma

Ewing's sarcoma (ES) is a small round blue cell neoplasm that occurs in adolescents. Many clinical features, staging requirements, and treatment algorithms are shared with osteosarcoma. Similarly, the main presenting complaints are

pain and a mass, but ES can be associated with systemic symptoms, like night sweats and fevers. XRs show a non-geographic, mottled, diaphyseal, or metadiaphyseal lesion with aggressive periosteal reaction (Fig. 16.3, images a and b). As with osteosarcoma, MRI of the entire bone determines the extent of disease and often shows a circumferential soft tissue mass. Histology shows sheets of small, round, blue cells which stain for CD99. The diagnosis is made by the presence of the EWSR1-FLI1 gene translocation [74]. Staging is the same as for osteosarcoma with the addition of a bone marrow biopsy, as diffuse hematogenous spread is possible. PET/CT can be used in lieu of a bone scan [65]. Treatment is similar, consisting of preoperative chemotherapy followed by en bloc, wide resection, and resumption of chemotherapy postoperatively. The chemotherapy regimen is VAC/IE (vincristine, Adriamycin, cyclophosphamide alternating with ifosfamide and etoposide) [75]. Unlike osteosarcoma, Ewing's sarcoma is radiosensitive. Thus, radiation therapy can be used for primary treatment of unresectable disease, which results in a higher local recurrence rate compared to surgical resection but does not affect overall survival [76]. Prognosis is similar to osteosarcoma with 5-year overall survival ranging between 65% and 75% [75]. Metastatic disease at presentation is again the greatest predictor of poor survival [75, 77]. Survival is also decreased with pelvic location, age >14, relapse—especially sooner than 2 years—and poor histologic necrosis with chemotherapy [71, 75, 77, 78]. Pathologic fracture does not appear to pose a challenge to overall survival as has been debated for osteosarcoma [79].

16.6.2.4 Chondrosarcoma

Chondrosarcomas (CS) are malignant, chondroid neoplasms that can arise de novo or secondary to other processes such as enchondromas. Pain is the main presenting symptom. XR will reveal the stippled calcifications of chondroid matrix with variable surrounding lucency (Fig. 16.2, image b). MRI will show the extent of the lesion within the bone and any soft tissue component. Histologically, the lesions will show blue, chondroid matrix with varying amounts of cellularity, nuclear atypia, and mitoses. Unlike other bone sarcomas, grades exist and include I, II, III, and dedifferentiated. A dedifferentiated chondrosarcoma will show abrupt transition from chondroid regions to areas of marked atypia and pleomorphism that more closely resemble an undifferentiated pleomorphic sarcoma or high-grade osteosarcoma [80]. Staging consists of an MRI of the affected bone and CT of the chest.

Treatment is dependent on subtype. Grade I lesions can be safely treated with aggressive intralesional resection, cementing, and fixation. There is no difference in local recurrence between intralesional and wide excision for grade I tumors [81, 82]. The remaining lesions are treated with en bloc, wide resection, and an appropriate reconstruction. As a lower-grade lesion overall, even locally recurrent disease can have a favorable outcome, with a 5-year survival of 74% [83]. Chondrosarcoma of the pelvis and extremity is not radiation sensitive. Chemotherapy is reserved for metastatic or dedifferentiated disease, as the effect is limited, with only 21% of dedifferentiated and 12% of conventional chondrosarcomas responding [84]. Prognosis is most dependent on the grade of chondrosarcoma and the presence of metastases. Five-year survival for grade I CS is over 90%, while for grade III CS, it is between 50% and 60% [85, 86]. Dedifferentiated chondrosarcomas have a limited prognosis with an overall 5-year survival rate between 7% and 24% [87, 88]. Metastatic dedifferentiated CS has a 2-year survival rate of only 10%, with no patients surviving to 5 years [88].

16.6.2.5 Undifferentiated Pleomorphic Sarcoma of Bone

Variants of soft tissue sarcomas can occur both as metastatic lesions and primarily in bone. These lesions are lytic on XR and contrast enhancing on MRI. Distinct to their treatment in the soft tissues, soft tissue sarcomas of bone are more chemosensitive. The classic example is undifferentiated pleomorphic sarcoma of bone. For these, the treatment is similar to osteosarcoma, consisting of preoperative chemotherapy and wide excision followed by postoperative che-

motherapy. Radiation can be used to further decrease the risk of local recurrence. Staging consists of MRI of the affected bone and CT of the chest. If the lesion is thought to be metastatic, whole-body imaging—PET/CT or whole-body MRI—should be considered to rule out a primary site of disease.

16.6.2.6 Metastatic Disease, Myeloma and Lymphoma

The differential for lytic lesions in patients over 40 is overwhelmingly 1 of 3 things: metastatic disease, multiple myeloma, or lymphoma. Primary sarcomas occur much less frequently. Any form of malignancy can have bony metastases, but the most common are breast, lung, thyroid, prostate, and renal. It is not uncommon for bone pain to be the first symptom of a widely metastatic malignancy. Thus, the role of the orthopedic surgeon in this setting is an adequate workup, which includes a thorough cancer history, full physical examination, lab work, appropriate imaging, and a tissue diagnosis. Lab work should include a CBC to evaluate for anemia and an increase in WBC, BMP to rule out the hypercalcemia that can occur with numerous bony lesions, SPEP and UPEP to rule out the immunoglobulin spikes seen in myeloma, TSH for thyroid, and PSA for prostate. Imaging consists of an XR and MRI of the affected bone; a CT of the chest, abdomen, and pelvis to evaluate for a primary site of disease; and a whole-body bone scan to assess the extent of bony involvement. Finally, a biopsy of the most easily accessible site can help make the diagnosis. Once a diagnosis is made, the involvement of appropriate specialists is initiated.

In the setting of metastatic disease, the goal is not margin-negative resection as local control of a single bony lesion will not have a survival benefit in widely metastatic disease. Lesions that do not immediately threaten bony stability can be observed on chemotherapy. Systemic treatment with bisphosphonates or denosumab can help prevent fracture. Symptomatic or destabilizing lesions are treated with intralesional resection and structural augmentation typically with cement and hardware. En bloc resection may be warranted if bony stability is sufficiently compromised. Radiation can be used for non-destabilizing lesions as a primary treatment, but should always be used postoperatively to prevent progression of disease and reoperation.

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Soft Tissue Tumors

17

James Pascal Norris IV

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the clinical and radiographic features of soft tissue tumors of the extremity.
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Common presentation of soft tissue tumors and the warning signs that suggest a malignancy
  2. Imaging modalities and characteristics of soft tissue tumors

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3. General treatment strategies of soft tissue tumors
4. Basic characteristics and biologic behavior of the more common soft tissue tumors seen in clinical practice

17.1 Clinical Presentation

As with bone lesions, a careful history and physical examination is vital to developing an appropriate differential and guiding further investigation. The most common presenting complaint for a soft tissue sarcoma is a painless soft tissue mass [1–3]. The duration of the mass and its growth pattern are key. Rapid growth is suggestive of a sarcoma, while stable size is suggestive of a benign one [4]. Growth of a previously stable mass may portend malignant transformation of a benign lesion, i.e., development of a malignant peripheral nerve sheath tumor within a known neurofibroma. While generally painless, certain entities themselves can be painful such as a schwannoma in a sensory nerve or desmoid fibromatosis. Others may cause secondary symptoms through “mass effect” if they grow so large as to compress neurovascular structures or restrict motion. Finally, internal necrosis or hemorrhage can cause rapid enlargement of a sarcoma, which can be quite painful.

Certain history items can accompany specific diagnoses. Waxing and waning size is common in ganglion cysts, which can increase due to inflammation of the underlying joint. Decrease in size would not be expected in the setting of a true neoplasm, benign or malignant. A history of trauma might suggest a hematoma, but this diagnosis must be settled upon carefully. The lack of symptoms means patients are often unaware of soft tissue masses until an unrelated event, such as a trauma, draws their attention to the area.

Physical examination is also vital to the differential. Size and depth are key findings. While not a very specific measure, size greater than 5 cm favors a sarcoma. Sarcomas have an average size of 10–11 cm at presentation [5, 6]. The same is true for depth below the fascia, which is detectable as a lack of mobility [4, 5]. However, 39% of sarcomas will be less than 5 cm and 36% will be superficial [4]. Consistency is also a helpful finding. Ganglion cysts can be firm and immobile but will transilluminate when light is applied and can be easily aspirated. Lipomas are typically soft; however, its low-grade cousin—well-differentiated liposarcoma—can have exam findings almost identical to that of a large lipoma. Sarcomas are generally firm and immobile, but the same can be said of desmoid fibromatosis. Local lymph nodes should be palpated for enlargement as some soft tissue sarcomas can metastasize to lymph nodes [7].

As evident above, soft tissue masses present a diagnostic dilemma as the history and exam findings overlap between benign and malignant diagnoses. The most important things for any orthopedist to understand are the red flag signs and symptoms that should prompt referral to a sarcoma specialist, namely, enlargement, size greater than 5 cm, and depth below the fascia. The combination of these three findings is 93% specific for a soft tissue sarcoma [4]. Still, no set or set of findings is pathognomonic; thus, imaging and biopsy are instrumental in making the correct diagnosis.

17.2 Radiologic Findings

17.2.1 Conventional Radiography (XR)

While XR can provide excellent bony detail, soft tissue detail is limited. Three major densities can be seen, including air, fat, and soft tissue. Soft tissue density is similar across muscles, organs, and fluid such as a joint effusion. Within these limitations, a soft tissue mass may alter the normal contours of muscle and subcutaneous tissue. A subcutaneous mass can be seen as a soft tissue density surrounded by normal subcutaneous fat. Conversely, an intramuscular lipoma can be seen as a fat density surrounded by normal

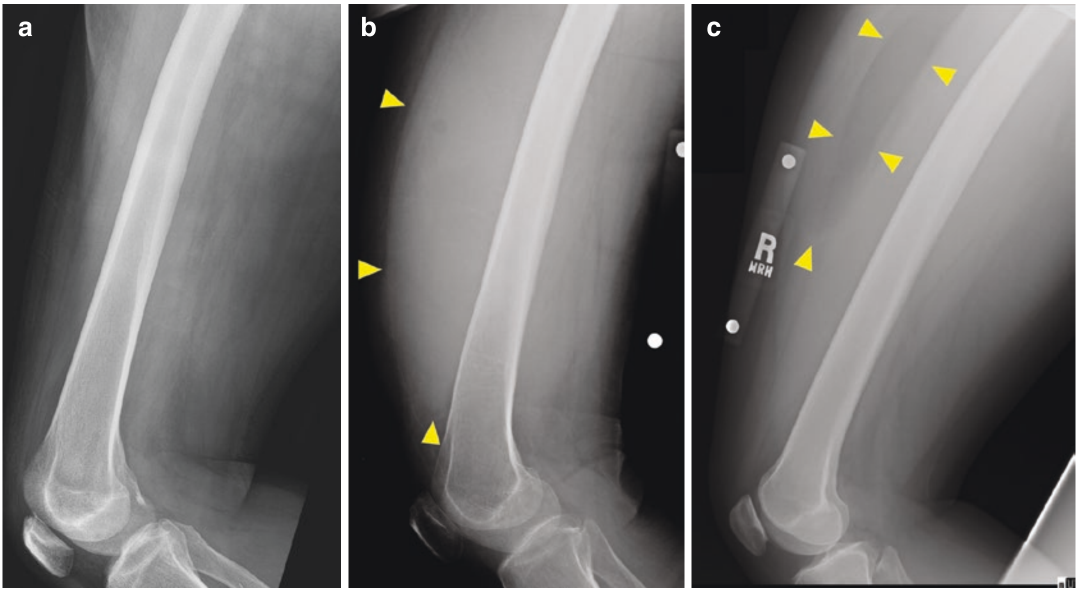

Fig. 17.1 Soft tissue densities on plain radiographs. Image (**a**) highlights the normal contours of the soft tissue shadow of the anterior thigh musculature and the thin overlying subcutaneous tissue shadow. By comparison, image (**b**) shows a markedly enlarged, ovoid shadow in a patient with a large anterior thigh soft tissue sarcoma. Image (**c**) shows a similarly enlarged shadow but with a fat density shadow within the anterior thigh musculature

muscle density (Fig. 17.1). Air is a rare finding and would not be expected except in the case of a fungating mass, after surgery, or when a gas-producing infection is suspected. Although nonspecific, intralesional calcifications are easily seen on XR.

17.2.2 Magnetic Resonance Imaging (MRI)

MRI is the key imaging study for evaluation of soft tissue masses. Understanding of the various sequences is vital for interpretation. All MRIs should be formatted into three orthogonal views—coronal, axial, and sagittal—for every sequence. T1 sequences are weighted such that fat is bright and soft tissue and fluid are dark. T1s also provides the most anatomic detail due to the sharp distinction between tissues types. It is vital for surgical planning, as the regular anatomy can be significantly distorted by the mass. This sequence will show the separation or lack thereof between a mass and vital structures, which is often seen as a "fat plane," i.e., a thin layer of fat between a mass and the structure in question (Fig. 17.2).

T2 sequences are weighted such that soft tissue is dark and water is bright. They are also typically fat suppressed, meaning that the brightness of fat is decreased to an intensity closer to that of the surrounding soft tissue. Fine anatomic detail is limited compared to T1 sequences; however, pathology is highlighted as the majority of soft tissue lesions have a significant fluid content. Thus, an abnormality will highlight brightly against the dark background of the soft tissue and fat. Short tau inversion recovery (STIR) sequences are a close cousin with even less anatomic detail but more stark contrast between fluid and non-fluid areas.

Finally, contrasted images are fat-suppressed, T1 sequences obtained after administration of gadolinium contrast. These images highlight well-vascularized, metabolically active areas. Comparison is facilitated by obtaining similar images before and after contrast administration. Several important things can be gleaned from these sequences. First, malignant lesions reliably take up contrast; thus, a lack of change from pre- and post-

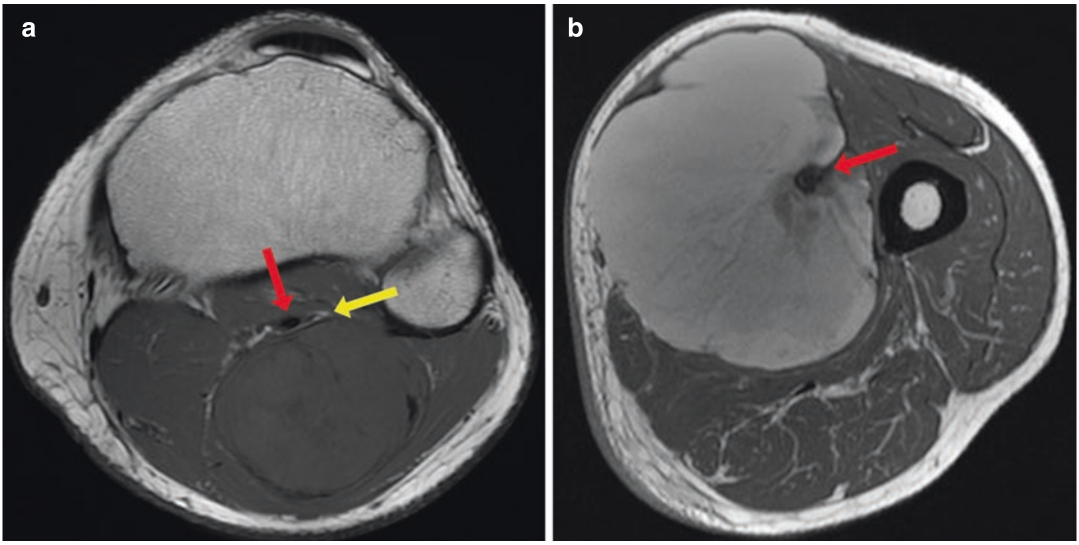

Fig. 17.2 Anatomic detail of T1 imaging. In image (**a**), the popliteal artery (marked by the red arrow) is separated from the mass (M) by a thin, T1 hyperintense plane of fat (marked by the yellow arrow). In distinction, the mass (M) in image (**b**) completely envelops the superficial femoral artery (marked by the red arrow)

contrast images is a key finding. This finding is useful in surveillance imaging when one is monitoring for a recurrence in a surgical field with distorted anatomy. Second, contrast enhancement can help distinguish benign and malignant lesions. For example, benign lipomas should not take up contrast. Mass-like contrast enhancement within a lipomatous lesion suggests a malignancy. Third, large and fast-growing masses can outgrow their blood supply and become necrotic, seen as areas of low contrast enhancement, typically central in the mass. In contrast, cysts and abscesses exhibit "rim enhancement," i.e., a thin area of contrast uptake along the lining of the lesion (Fig. 17.5) [8, 9]. Despite these findings, one should remember that MRI signal characteristics can be histologically nonspecific; if imaging findings are not definitive, a biopsy may be necessary to reach an appropriate diagnosis.

A good pattern for reading an MRI is a coronal T2 followed by the axial T1 and T2 images and finishing with contrasted images. A coronal T2 will starkly highlight pathologic areas and focus further evaluation to the appropriate location. With this localization, the axial T1 images can be used to determine the exact location of the mass in relation to vital structures. Finally, contrasted images can be helpful to further determine the exact extent of the mass as perilesional edema can be difficult to distinguish from the mass itself on other sequences. Contrasted coronal images are useful to determine the relationship of the mass to normal anatomic landmarks, which allows the surgeon to plan his or her incision intraoperatively.

Finally, whole-body MRIs have gained importance as an alternative to PET/CT in malignant lesions with an unpredictable metastatic pattern, of which myxoid liposarcoma is a classic example [10–12].

It is important to understand the difference between a determinate lesion and indeterminate one. Determinate lesions, such as a ganglion cyst or lipoma, can be definitively diagnosed based on MRI findings, or those of other studies, which obviates the need for a tissue diagnosis. In distinction, indeterminate lesions cannot be definitively diagnosed on imaging alone and should be followed with serial imaging or biopsied for definitive diagnosis [8, 9].

17.2.3 Computed Tomography (CT)

As a digitally synthesized "stack" of XRs, CTs offer similar soft tissue definition with added three-dimensional detail. The limited distinction between tissue types on CT makes this a less useful primary imaging study for soft tissue lesions. The addition of contrast can highlight blood vessels and areas of increased vascularity, but the anatomic data remains inferior to that of an MRI. Regardless, this may be the only option in patients who are unable to get MRIs, such as those with pacemakers or cochlear implants. However, chest CTs are the study of choice for lung metastasis surveillance.

17.2.4 Positron Emission Tomography (PET)

Often coupled with an overlain CT, PET imaging relies on the administration of a radiotracer attached to a glucose molecule, ^{18}F-fluorodeoxyglucose (FDG), which is taken up by metabolically active tissue. While PET has limited utility in the primary evaluation of soft tissue masses, it can be useful in the surveillance of soft tissue sarcomas that have the potential for non-chest metastases. Summarized in the pneumonic "RACES," there are five main sarcomas that have the potential for lymph node metastases for which PET imaging can be useful: rhabdomyosarcoma, angiosarcoma, clear cell sarcoma, epithelioid sarcoma, and synovial sarcoma [7]. Further, whole-body PET imaging can be useful in identifying a primary source of disease if a sarcoma is first recognized in its metastatic form such as from a lymph node or lung metastasis. PET has not supplanted traditional chest imaging because the resolution of the CT portion is lower than that of a dedicated chest CT and PET has limited ability to highlight small pulmonary nodules [13].

17.3 Biopsy

For indeterminate soft tissue lesions, biopsy is a key next step in determining a tissue diagnosis. There are several biopsy methods ranging from least to most invasive: fine needle aspiration, core needle biopsy, incisional biopsy, and excisional biopsy.

Fine needle aspiration is simple and quick and provides rapid results [14]. However, the sample is often small and the microscopic architecture of the mass is lost via the aspiration. Thus, diagnostic yield is lower than with other biopsy techniques [15]. While the diagnostic information may be limited, the finding of malignant cells can be a useful and quick first step in the diagnostic pathway. Further, it can be sufficient to make the diagnosis of a local recurrence or a lung metastasis, i.e., where the diagnosis is known and cytology can be compared to previous slides.

Core needle biopsy is a more useful diagnostic tool because the larger needle and lack of aspiration samples a larger amount of tissue and preserves the microscopic architecture allowing assessment of the morphology of the lesion. The imaging guidance used, be it ultrasound, CT, or MRI, helps prevent sampling area. As such, the diagnostic accuracy ranges from 70% to 93% [14, 16–18]. Benign lesions are less likely to allow for definitive diagnosis; thus, the corresponding clinical and radiologic information must be synthesized to aid in diagnosis [16, 17]. It is also oncologically safe. The biopsy tract is seeded in only 0.8% of cases, compared to 12% for open biopsy [19], and resection of the tract does not affect the rate of local recurrence [20]. Thus, core needle biopsies offer an accurate method of diagnosis that can be performed with local anesthesia and does not affect local recurrence rates.

Incisional biopsies involve making a surgical incision under general anesthesia and obtaining an adequate sample for diagnosis. There are important principles to follow when performing open biopsies as this can introduce significant morbidity if performed poorly [21]. The incision must be in line with that of the resection so that the biopsy tract can be easily resected along with the mass. Limited dissection and meticulous hemostasis must be carried out to limit seeding of the surrounding tissue. An adequate and representative sample must be obtained to prevent the need for further biopsy. An open biopsy should be performed by the treating specialist to prevent complication, a referral

pattern that has been shown to decrease seeding of the biopsy tract [19].

Excisional biopsies involve removing a lesion en bloc prior to a definitive diagnosis being made. This is typically reserved for smaller lesions that would be difficult to accurately and safely biopsy with a needle. As previously noted, an appreciable percentage of sarcomas are superficial and small. As such, proper technique for excisional biopsy dictates that a wide, i.e., negative, margin be taken with the mass in case a malignancy is present. Further, any lesion that is excised from any part of the body *must* be sent for pathologic analysis to prevent missing a malignancy.

17.4 Pathology

An in-depth exploration of all the factors that lead to a specific pathologic diagnosis is outside the scope of this chapter. However, certain basic elements are helpful to understand. Descriptive assessment of slides treated with the standard hematoxylin and eosin (H&E) staining is the first step in pathologic diagnosis. Cell types are described, such as spindled, epithelioid, and round cells. The extracellular matrix or stroma is described such as fibrous, myxoid, osteoid, or chondroid. Organized structures can be seen such as vascular or lymphatic channels or mature bone. Each of these findings can help narrow the diagnosis.

Certain general characteristics of the cells can give a clue to the diagnosis and its relative aggression. Pleomorphism can be seen, which is the degree of variability in the shape and size of the tumor cells. More pleomorphism speaks to a more aggressive diagnosis. Low-grade or benign lesions tend to have more uniform cells. Nuclear atypia can also be seen, which is the variable size, shape, number, and makeup of the nuclei of the tumor cells. Mitotic figures are evaluated and represent cells in the process of division. Non-neoplastic, benign, or low-grade lesions should have few if any dividing nuclei. Necrosis, or areas of dead cells, can also be seen which speaks to a more aggressive, fast-growing lesion that has outgrown its blood supply. All of these factors are used to help grade a given mass and summarized in Fig. 17.3.

More specific elements of the pathology are then used to help determine the specific type of lesion. One of these elements is the extracellular matrix produced by the lesional cells. Fluid-filled vacuoles, collagen fibrils, and loose myxoid stroma are all examples of the numerous morphologic appearances of soft tissue lesions (Fig. 17.4). Cellular ultrastructures, such as the abnormal blood vessels seen in angiosarcomas, can also give a clue to the specific diagnosis if present.

Special stains can be used to help distinguish one lesion from another. The list of stains is long; thus, it is important to formulate a diagnosis from

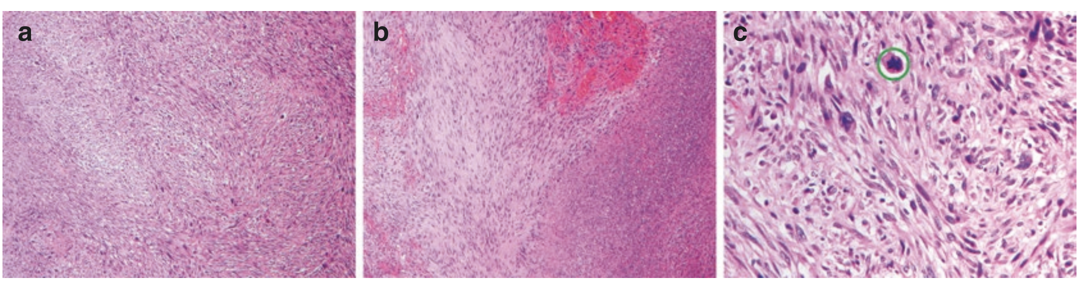

Fig. 17.3 Grading elements for soft tissue lesions. Image (**a**) shows the low-power view of an undifferentiated pleomorphic sarcoma. Note the elongated, "spindle" shape of the cells. Spindle cells are a common cellular morphology seen in soft tissue masses. Image (**b**) shows another low-power image from the same lesion. The bottom right of the image shows an area of necrosis with loss of cellular architecture and dense red color. Image (**c**) is a higher power image which highlights three key findings that suggest a higher-grade lesion: cellular pleomorphism (cells of variable shapes and sizes), nuclear atypia (irregular nuclear size and shape), and mitotic figures (cells in the process of division with dense, dark chromatin, here marked with the green circle)

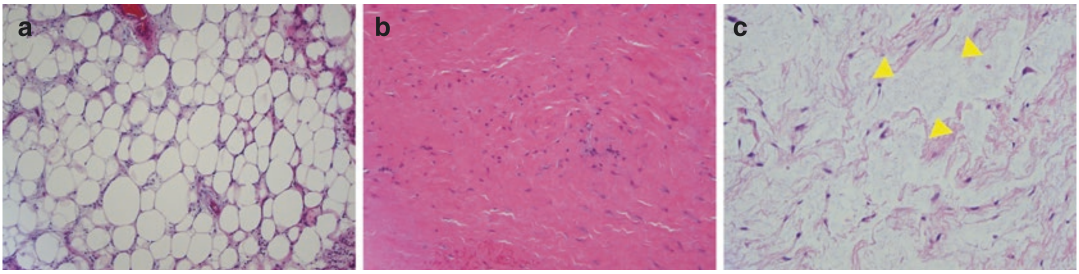

Fig. 17.4 Types of extracellular matrix. Images (**a**) through (**c**) are low-grade or benign lesions with examples of classic matrix production. Image (**a**) shows a well-differentiated liposarcoma with the characteristic large, clear vacuoles of lipomatous tissue. Image (**b**) shows a benign fibroma and the characteristic wavy, eosinophilic collagen fibrils seen in fibrous lesions. Image (**c**) is a benign myxoma showing the loose, acellular, blue myxoid stroma seen in a variety of soft tissue lesions with a myxoid component

the morphology of the lesion to help guide the stains chosen for a given lesion. Examples include S100 for nerve sheath tumors or desmin for skeletal muscle tumors. Further, genetic analysis via fluorescent in-situ hybridization (FISH) or polymerase chain reaction (PCR) testing can show characteristic mutations and translocations such as SS18-SSX in synovial sarcomas or MDM2 in well-differentiated liposarcomas.

Other important features can be determined from the pathologic specimen, apart from the specific diagnosis. Grading is an important pathologic factor. Criteria exist for the various tumor types, but grading typically involves pleomorphism, atypia, mitoses, and necrosis. Increasing grade portends a worse prognosis for the patient.

Margins are another vital aspect of pathologic analysis and are assessed when evaluating specimens that have been resected. As will be discussed later, margin status directly impacts the chances of local recurrence. In general, margins are designated in one of three ways. An R0—"negative" or "wide"—margin means that there is a continuous layer of normal tissue surrounding the mass, ensuring that no tumor cells were left behind. The exact definition of a wide margin has been debated, but the key distinction is that a margin is negative. These are both grossly and microscopically negative. An R1—"marginal"—margin means that there is no normal tissue surrounding the mass but that the edge of the specimen is the edge of the mass itself. This can be described as grossly negative, but microscopically positive, and suggests that microscopic disease may remain in the surgical field. Finally, an R2—"intralesional" or "contaminated"—margin means that the mass itself was violated and the edge of the specimen is within the mass itself. This suggests that the margin is both grossly and microscopically positive and that gross disease likely remains in the surgical bed [22].

17.5 Staging

Once the diagnosis has been made, the next step in clinical evaluation of patients with soft tissue lesions is staging. Staging is vital for malignant lesions with metastatic potential to determine the extent of disease, which informs prognosis and guides treatment decisions. Non-neoplastic and benign lesions do not warrant staging evaluation and can be treated as isolated, local lesions.

The first and most important imaging study for soft tissue sarcoma staging is a dedicated MRI with and without contrast of the affected anatomic area. This helps determine the size of the lesion and the anatomic areas involved. A broad enough field of view is necessary to accurately assess the extent of a lesion. A good rule of thumb for the extremity is to image the joint above and below a given lesion. The next step is evaluation for metastases. Although any soft tissue sarcoma can metastasize to any location, the majority will metastasize to the lungs. Thus, a chest CT with contrast is

necessary. Any nodule over 1 cm in the setting of a soft tissue sarcoma is essentially diagnostic of a metastasis. Lesions less than 1 cm are considered indeterminate. The risk of metastases for lesions between 5 and 10 mm is around 1/3, while the presence of nodules <5 mm has no effect on prognosis [23]. As discussed earlier, PET/CT is not sensitive enough to assess pulmonary nodules, and its addition to the standard staging studies will add additional information in less than 5% of cases [24]. However, as discussed, whole-body imaging can be useful in certain circumstances such as PET/CT for sarcomas with a nodal predilection or whole-body MRI for myxoid liposarcomas.

Based on the results of these studies, an overall stage can be given to the patient's disease, which in turn helps determine prognosis. Various staging systems exist, but the American Joint Committee on Cancer (AJCC) is commonly used in the USA. Regardless of the system, staging incorporates tumor size, tumor grade, and extent of disease both locally and distantly. Not surprisingly, a 3 cm, low-grade sarcoma without metastases has a much better survival rate than a 20 cm, high-grade sarcoma with diffuse metastases. Staging systems attempt to codify this difference.

If a soft tissue mass is found to represent a metastasis, such as a carcinoma or lymphoma, appropriate imaging is warranted to determine the primary site of disease. Carcinoma should prompt a CT of the chest, abdomen, and pelvis. Melanoma warrants a thorough physical examination and whole-body PET/CT. Lymphoma requires lab work and a bone marrow biopsy.

17.6 Treatment Strategy

Once a diagnosis has been made, the clinician is then able to determine an appropriate treatment strategy. The definitive treatment for most soft tissue lesions, either benign or malignant, is surgical resection. No adjuvant therapy is able to completely eradicate local disease; thus, the decision for or against surgery is typically the first and most important one.

17.6.1 Observation

Observation is a reasonable strategy for small lesions that are not changing in size and are asymptomatic, such as a lipoma or neurofibroma. If stable and the diagnosis is sure, benign lesions pose no survival risk to the patient. In this scenario, removal would be elective and at the request of the patient. The so-called active surveillance, with serially obtained imaging, may be warranted for soft tissue masses that have a chance to undergo malignant transformation. A good example is neurofibromatosis in which the numerous neurofibromas all have the opportunity to undergo sarcomatous transformation. Patients with such lesions or conditions should be followed regularly both clinically and radiographically to monitor for changes in their lesions.

17.6.2 Surgical Resection

Surgery is indicated for patients in the setting of a diagnosed malignancy but may also be warranted for benign lesions that are painful such as a schwannoma, are unsightly to the patient such as a large lipoma, or have shown growth after years of stability. The type of resection is dependent on the correct diagnosis. Benign lesions can be safely removed in a marginal fashion, as the likelihood of recurrence is low with complete resection. In contrast, sarcomas must be removed in a margin-negative fashion. Much energy has been expended in the literature to determine the significance of margin status, and the exact definition of an adequate margin has been debated for many years and is outside the scope of this chapter. However, it is clear that an R1 or R2 resection conveys an increased risk of local recurrence as compared to an R0 resection [25–27].

Once a mass has been removed, the soft tissue reconstruction is determined by the extent of the resection. If adequate muscle is available in the surgical bed, a primary closure can be achieved. If a void is present, a muscle flap can be utilized, either a local, pedicled flap, such as a gracilis flap in the thigh, or a distant, free flap, such as an anterolateral thigh myocutaneous flap. If a large

amount of skin is removed, the underlying muscle may be covered with a skin graft, either full or split thickness. The type of closure does not appear to alter surgical outcomes so the choice is strictly based on necessity [28–31]. However, the need for flap closure correlates with increasing tumor size and histologic grade; thus, these patients are at a higher risk for a worse outcome [28]. Rarely, bone is directly involved and must be resected en bloc with the soft tissue lesion. Reconstruction would follow similar principles as discussed in the previous chapter.

17.6.3 Adjuvant Therapy

17.6.3.1 Chemotherapy

Chemotherapy has a narrow scope of benefit in the treatment of soft tissue lesions. Some benign, but locally aggressive, lesions can be treated with systemic chemotherapy, most notably desmoid fibromatosis and PVNS. Both have a high local recurrence rate and can require multiple, morbid surgeries; thus, exhausting non-operative chemotherapeutic options is warranted. Some soft tissue sarcomas are particularly sensitive to chemotherapy, including synovial sarcoma and alveolar rhabdomyosarcoma, in which cases chemotherapy is included in the standard treatment regimen [32, 33]. For soft tissue sarcomas as a whole, however, chemotherapy will be effective in only about 25% of patients and will not affect overall survival [34, 35]. Therefore, it is typically reserved for the case of particularly sensitive, high-grade, large, or metastatic lesions.

17.6.3.2 Radiation

For soft tissue sarcomas, radiation is a mainstay of local treatment. While no soft tissue sarcoma can be treated with radiation alone, its use significantly decreases the rate of local recurrence [36–38]. Preoperative and postoperative radiotherapy are equally effective adjuvants but each carries its own risks and benefits. Preoperative treatment allows for a lower dose and a more focused field of treatment. However, the risk of postoperative wound complications increases significantly [30, 31]. Alternatively, postoperative treatment decreases the risk of wound healing complications, but requires a higher dose of radiation, a broader field that includes the entire surgical field and is more likely to cause tissue fibrosis and pain. All forms of radiation can lead to skin toxicity, lymphedema, osteonecrosis, and rarely, post-radiation sarcoma [39, 40]. Because of these risks, radiation is rarely if ever used for benign conditions. In cases of small or superficial lesions, radiation therapy may also be deferred.

17.7 Non-neoplastic Conditions

Several non-neoplastic conditions can present as soft tissue masses in the extremity. As before, accurate diagnosis is key to appropriate treatment. Falsely diagnosing a sarcoma as one of these conditions can lead to non-oncologic resection of a soft tissue sarcoma. Thus, if any doubt in the diagnosis exists, a biopsy or referral to a sarcoma center is warranted. Of note, several metabolic and inflammatory conditions can cause soft tissue masses.

Ganglion cysts and *synovial cysts* are periarticular cysts that commonly occur in the wrist and knee, but can occur in any location throughout the body. They are often associated with pain and can be firm and immobile. They will typically wax and wane in size and should transilluminate on exam if adequately superficial. Ganglion cysts lack an epithelial or synovial lining and are thought to be caused by extravasation of synovial fluid from a weak point in a joint capsule causing a reactive, fibrous lined, mucin-producing structure. They are filled with gelatinous mucin which can be easily aspirated. Synovial cysts are true outpouchings of a nearby joint lining due to chronic inflammation and are filled with synovial fluid. In both, MRI will show a uniform, T2 hyperintense mass with thin, rim enhancement (Fig. 17.5). Any irregularity in imaging such as internal signal or complex contrast enhancement should prompt a biopsy. Appropriately diagnosed, they can be aspirated, injected with steroids, or resected [41].

Abscesses can be large and form a mass-like swelling in an extremity. They can also have sig-

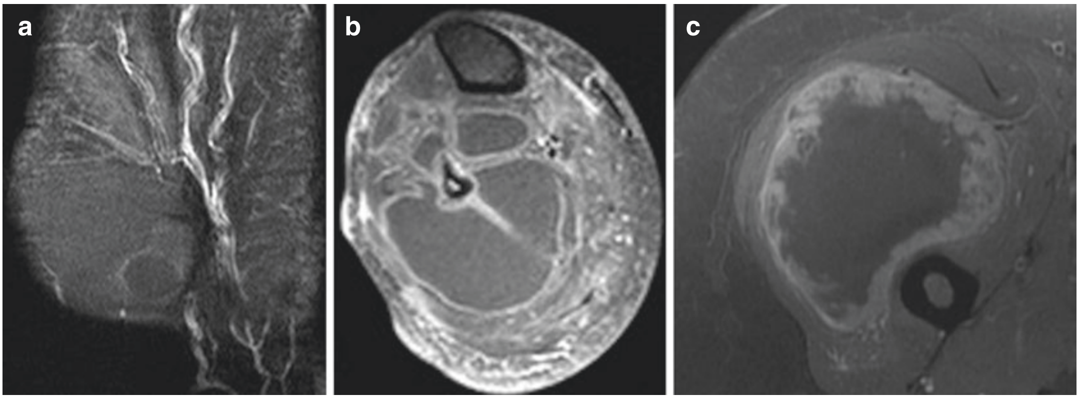

Fig. 17.5 Rim enhancement versus enhancement of a centrally necrotic sarcoma on contrasted MRI images. Image (**a**) shows thin, regular "rim enhancement" of a ganglion cyst of the thenar eminence. Similarly, image (**b**) shows a similar appearance with enhancement of the internal loculations of a periosteal abscess surrounding fibular osteomyelitis. In contrast, image (**c**) shows the thicker and more irregular peripheral enhancement of a centrally necrotic soft tissue sarcoma of the thigh

nificant surrounding edema and internal septations that make MRI interpretation complex. Unlike a soft tissue sarcoma, they will also show thin, peripheral rim enhancement (Fig. 17.5). Fluid will typically be thick and purulent as opposed to the thin, dark fluid of a centrally necrotic or hemorrhagic soft tissue sarcoma. Cultures will generally be positive, further distinguishing this from a soft tissue sarcoma. However, the old adage "culture what you biopsy and biopsy what you culture" can be of use in this setting to definitively rule out a soft tissue malignancy. Incision and drainage is the appropriate surgical treatment.

Hematomas can be a source of confusion in the setting of a soft tissue mass. Patients may recall a trauma or be on blood thinners, but often do not recall an inciting event and have no predisposing reason to bleed. The hematoma may be painful or painless. MRI imaging can show a heterogenous, variably contrast-enhancing mass with surrounding edema. Repeating an MRI over a short interval can be a helpful diagnostic tool as hematomas undergo a characteristic evolution of findings on T1 and T2 sequences that can make the diagnosis (Fig. 17.6). If absent or more concerning features are seen, a biopsy or referral to a sarcoma center should be undertaken [42, 43].

Myositis ossificans (MO) is the calcification of muscle that can occur spontaneously or after a trauma. This too can appear heterogenous and contrast enhancing and have a large amount of surrounding edema. Short-interval XR and CT can be useful in the diagnosis as the area will calcify peripherally and do so in a fairly uniform pattern and time frame (Fig. 17.7). If the presumed area of MO deviates from this pattern, a biopsy or referral should be sought [3, 42].

17.8 Benign Lesions

Benign soft tissue neoplasms are more common than malignant ones by a ratio of 60–40% [44]. The most common benign lesions are lipomas and lipoma variants, fibromas or fibrohistiocytic lesions, vascular malformations, neurofibromas, schwannomas, and myxomas [44, 45]. This section will seek to briefly describe several of these common lesions and a few others pertinent to orthopedic surgeons.

Lipomas are benign, fatty neoplasia that can occur anywhere in the body. As mentioned, XRs can show a fat density within a muscular compartment, but are typically unremarkable. MRI can be diagnostic and will show a homogenous, T1 hyperintense lesion that is

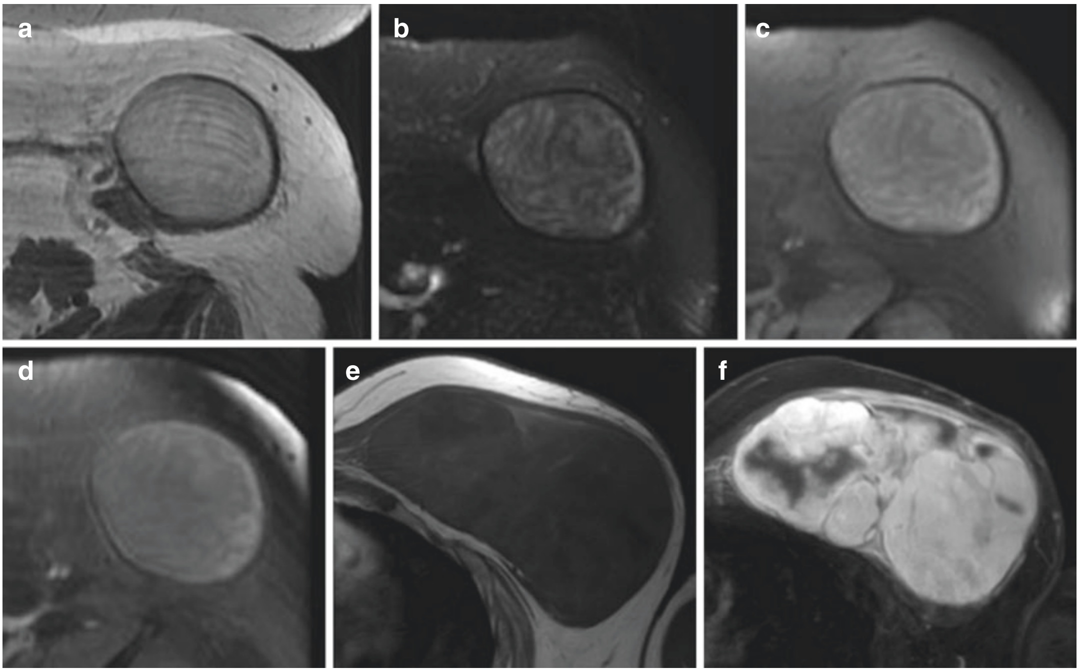

Fig. 17.6 Hematoma versus soft tissue sarcoma. Images (**a**–**d**) are the MRI images of a chronic hematoma of the abdominal wall caused by subcutaneous blood thinner injections. Note the fairly homogenous internal signal with both a T1 hypointense (**a**) and a T2 hypointense (**b**) rim around the mass. There is no enhancement from pre-contrast (**c**) and post-contrast (**d**) images. In contrast, images (**e**) and (**f**) are the T1 (**e**) and post-contrast (**f**) images of a large myxofibrosarcoma of the pectoralis muscle thought to be a hematoma clinically. Note the heterogeneity and lack of hypointense rim around the mass that distinguishes this from a hematoma

isointense to the subcutaneous fat. They should not have internal T2 signal nor take up contrast. Higher-grade liposarcomas will have marked heterogeneity on imaging that should prompt a further workup (Fig. 17.8). However, well-differentiated liposarcomas (WDLS) can appear very similar to lipomas on imaging. Key criteria to suggest WDLS are age greater than 60, lower extremity location, size greater than 10 cm, and non-fatty areas on MRI [46, 47]. Stable, painless lipomas can be observed for growth. Enlarging or symptomatic lesions or those that meet the above criteria should be removed in a marginal fashion.

Desmoid fibromatosis is a benign but locally aggressive soft tissue neoplasm with an infiltrative growth pattern that makes a margin-negative resection difficult and the risk for recurrence high [48, 49]. This presents as a firm mass on examination with variable amounts of discomfort. MRI will show a heterogenous T2 hyperintense and contrast-enhancing mass with ill-defined borders. Mature areas will have low T1 and T2 signal similar to tendon and bony cortex consistent with the dense fibrous tissue that makes up the lesion. Histology will show a moderately cellular collection of uniform, slender, spindle cells separated by collagen with little cell-to-cell contact [48]. Treatment strategies have included observation, anti-inflammatories, cytotoxic chemotherapy, radiation therapy, and surgical resection. All have a high recurrence rate and risk of complications, and the rate of stability after a period of observation ranges between 60% and 92% [49]. Therefore, the least aggressive treatment strategy should be exhausted first.

Hemangiomas are lobulated masses of capillaries that can regress spontaneously, while *vascular malformations* are abnormal nests of vascular structures—arterial, venous, lymphatic, or mixed—that grow proportionately with patients as they age [50]. XR can show characteristic phleboliths, and MRI will demonstrate a

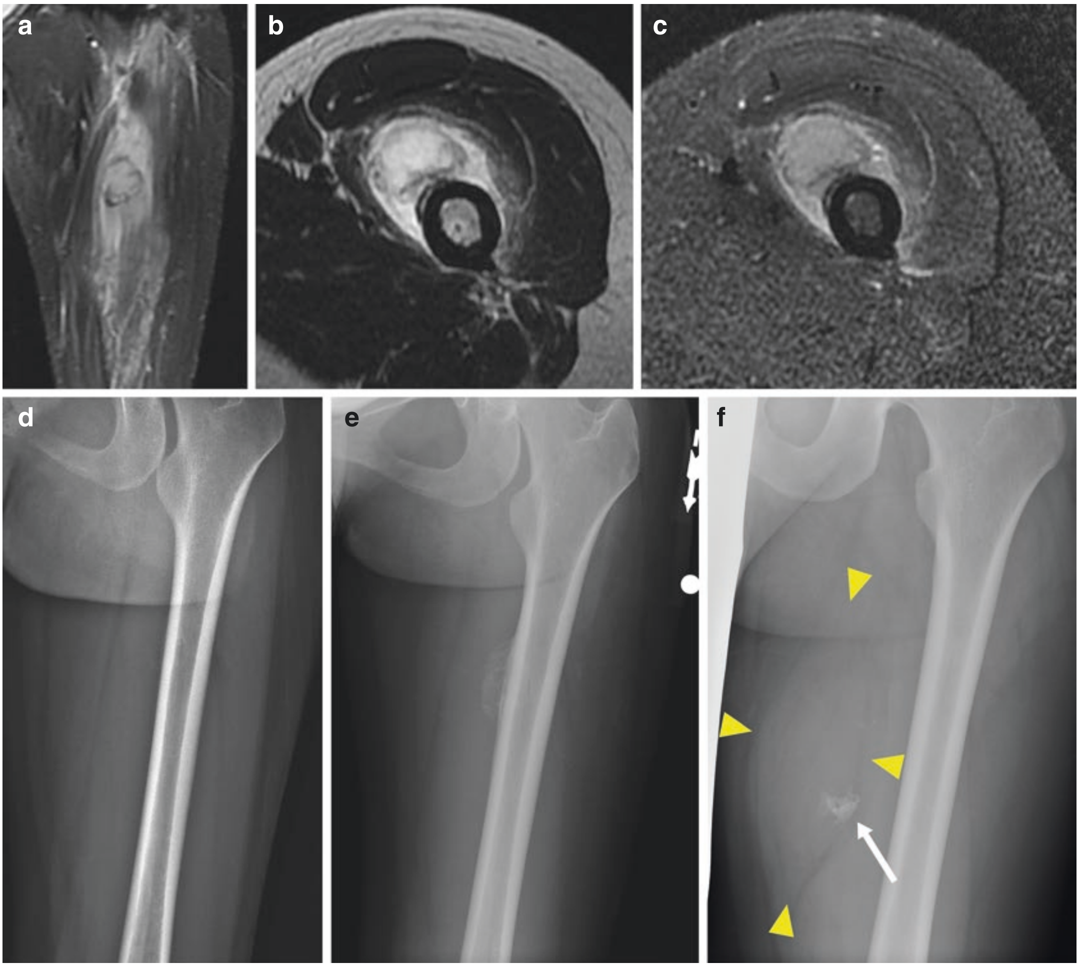

Fig. 17.7 Myositis ossificans. Images (**a**–**c**) are the MRI images of a patient who presented with a mass after bumping her thigh on a counter. Note the significant surrounding edema. Image (**d**) is her initial XR revealing a very subtle calcification. Image (**e**) is an XR taken 2 months later which shows the characteristic progression of peripheral calcification around the mass seen on MRI. MRI images show the T1 and T2 hyperintense halo at the periphery of the mass consistent with this area of calcification. Contrast this to image (**f**), which shows a soft tissue sarcoma (highlighted by the yellow arrows) with a central area of calcification (white arrow) arranged in a more haphazard and central pattern

lobulated, worm-like pattern with high T2 signal and marked contrast enhancement. Vascular malformations can cause swelling and pain, but have a high rate of recurrence making surgical intervention less beneficial for patients. As such, symptomatic treatment, systemic medications, and percutaneous embolization are favored over surgical resection [51].

Schwannomas are benign, slow growing, typically isolated lesions that occur within peripheral nerves. They can be painful if large enough or approximated to a sensory nerve. MRI will show a homogenous, T2 hyperintense lesion with a characteristic comet-tail or egg-on-a-string appearance representing the normal nerve tapering above and below the lesion (Fig. 17.9). Histology will show a biphasic pattern with areas of hypercellularity and palisading nuclei (Antoni A) mixed with hypocellular, myxoid areas (Antoni B) and will stain with S100 [52]. They

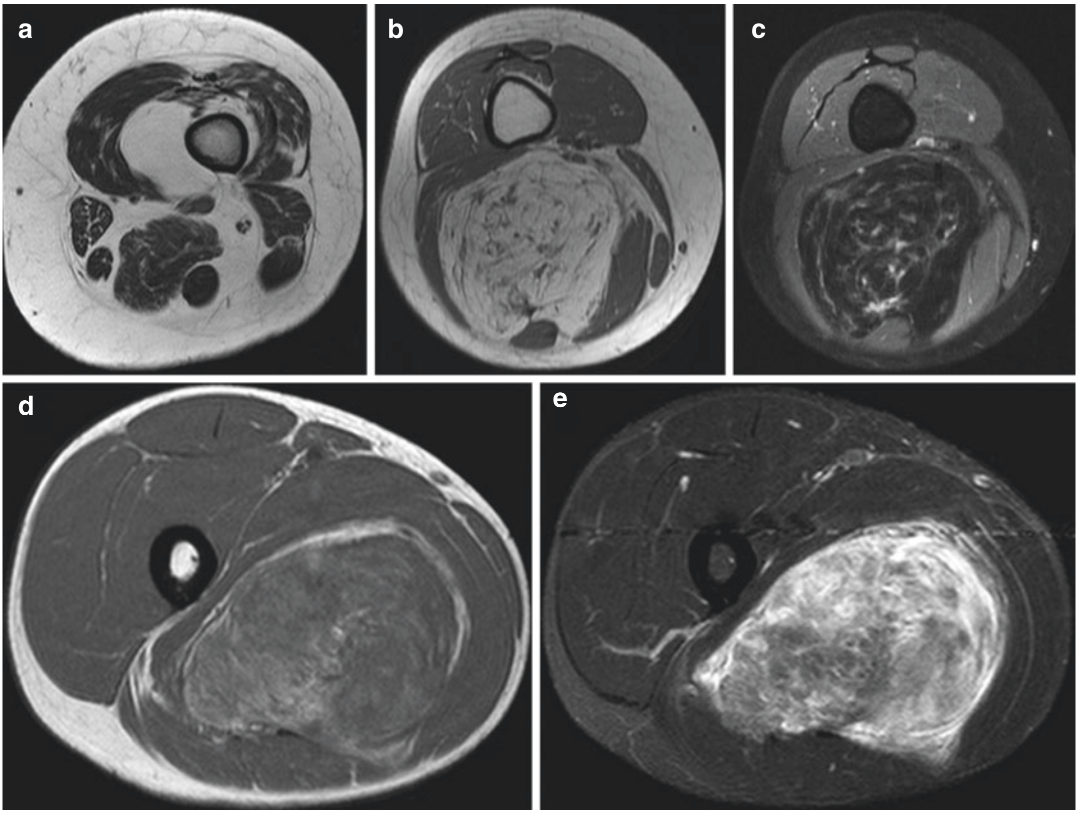

Fig. 17.8 Spectrum of lipomatous lesions on imaging. Image (**a**) is the T1 MRI sequence for a benign lipoma of the thigh. Note that the T1 signal within the lesion is homogenous and identical to that of the subcutaneous fat. Images (**b**) and (**c**) are the T1 and T2 images for a well-differentiated liposarcoma. The majority of the mass remains T1 hyperintense but there are intertwining areas of T1 hypointensity (**b**) with abnormal T2 hyperintensity (**c**). Images (**c**) and (**e**) are the T1 and T2 images of a true liposarcoma. Note that there is little T1 hyperintensity, i.e., fat, within the lesion with the majority being T2 hyperintense

can be removed in a marginal fashion that typically involves opening the epineurium. While the risk of recurrence is minimal if not zero, surgery has a moderate risk of transient and potentially permanent nerve deficit [53, 54]. Observation is reasonable if the diagnosis is sure, and the lesion is stable and asymptomatic.

Similar to schwannomas, *neurofibromas* are slowly enlarging, typically painless masses of a peripheral nerve. Imaging will have similar findings to a schwannoma. A target sign—central decreased T2 signal on axial T2 images—may be present. Histology will show interlacing bundles of spindle cells with wavy nuclei mixed with strands of collagen and variable amounts of mucoid material. Excision is again dictated by symptoms or concern for malignant transformation due to rapid growth or large size [52]. This is of particular concern in patients with neurofibromatosis for whom the rate of transformation is between 1% and 13% [55, 56].

Pigmented villonodular synovitis (PVNS) is a partially reactive, partially neoplastic synovial proliferative disorder that can occur in a contained, “localized” form or a widespread, “diffuse” form in any synovial joint, classically the knee. They can cause intra-articular bleeding, which results in an effusion, pain, and, over time, joint destruction. XRs will show a large joint effusion as well as arthritis and periarticular erosions in advanced cases. MRI reveals an intra-articular lesion with low signal on both T1 and

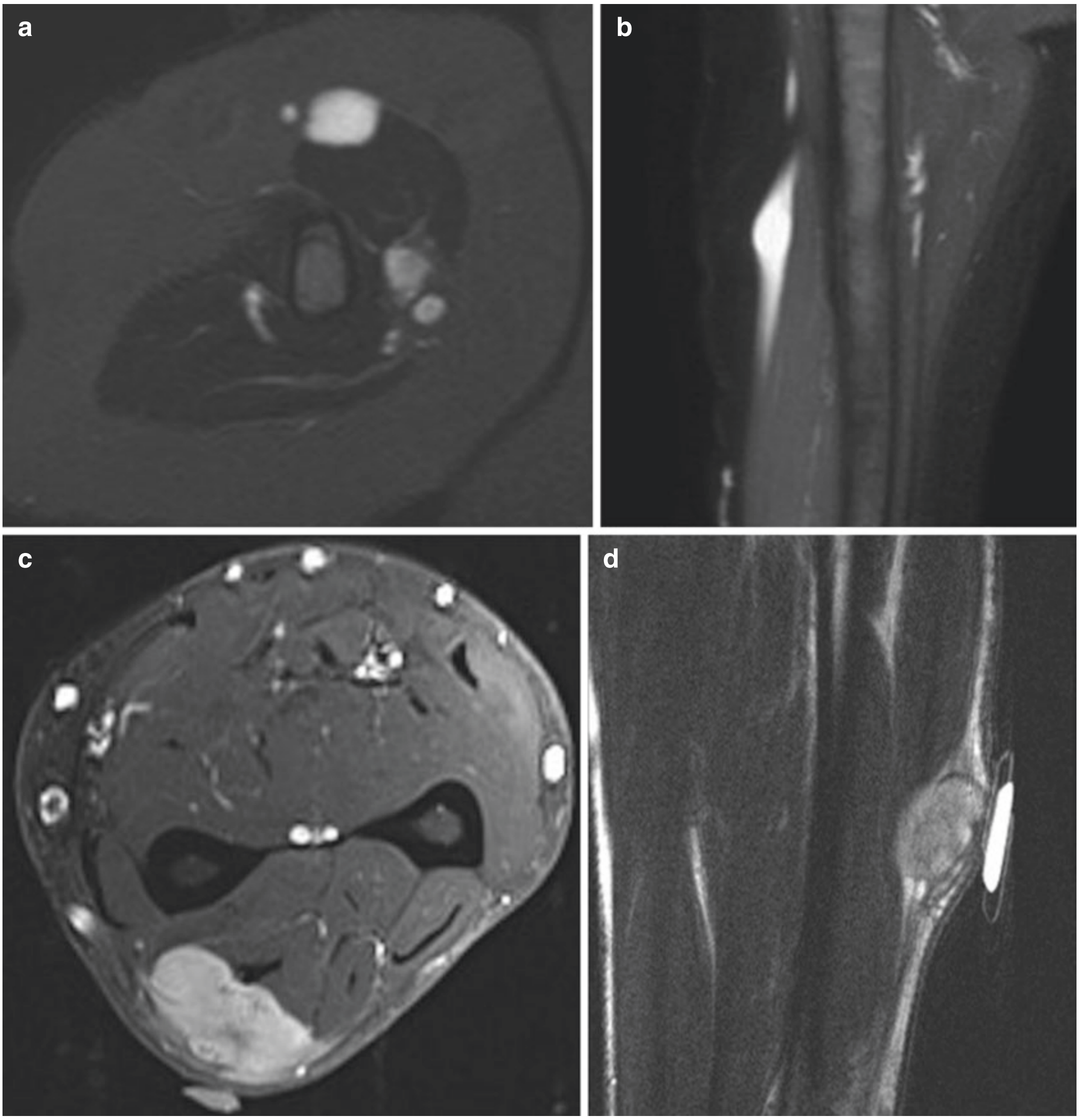

Fig. 17.9 Schwannoma versus soft tissue sarcoma. Images (**a**) and (**b**) are the MRI images of a benign schwannoma of the upper arm. Note the homogenous signal with the characteristic "egg-on-a-string" or "comet-tail" appearance on the sagittal image (**b**). Images (**c**) and (**d**) are those of a high-grade sarcoma of the forearm that was mistaken for a schwannoma. Note the heterogenous signal, infiltrative growth pattern, and discrete mass appearance on the sagittal image (**d**)

T2 images (Fig. 17.10). Histology reveals uniform, bland-appearing, mononuclear cells with scattered giant cells and hemosiderin staining [57]. Synovectomy is the mainstay of treatment either open or arthroscopic, both of which have a high rate of recurrence ranging between 20% and 50% [58–60]. Definitive treatment is with a joint replacement if indicated and feasible.

17.9 Malignant Lesions

Numerous soft tissue sarcomas exist, each with different subtypes and histologic grades. The most common soft tissue sarcomas in variable order depending on the analysis are undifferentiated pleomorphic sarcoma, liposarcoma, leiomyosarcoma, malignant peripheral nerve sheath

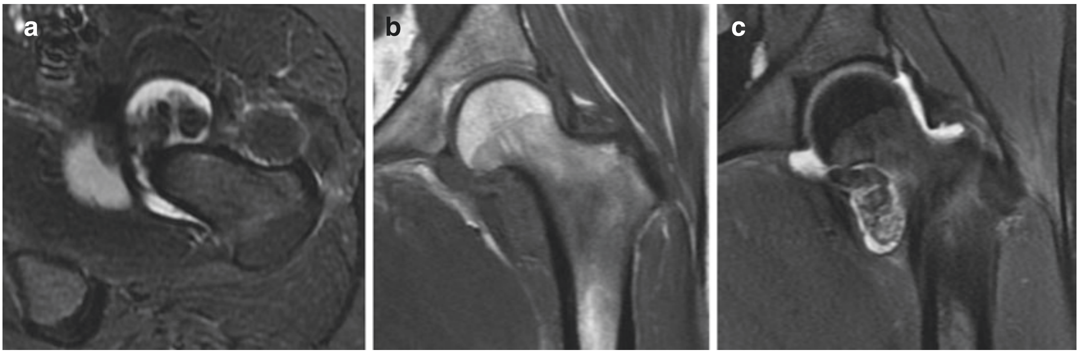

Fig. 17.10 PVNS. Images (**a**) through (**c**) are those of PVNS of the left hip. Note the intra-articular location, lobulated appearance, and large joint effusion on T2 imaging (**a** and **c**). There is characteristically low signal intensity on both T1 (**b**) and T2 images

tumor, synovial sarcoma, and myxofibrosarcoma [61, 62]. Barring a few exceptions, the treatment and staging algorithm are uniform, regardless of the specific diagnosis. The majority of this has already been discussed previously, but will be summarized again here.

If a soft tissue sarcoma is confirmed on biopsy, staging should include an MRI with and without contrast of the affected area including a wide enough field of view to facilitate relationship to palpable landmarks and a CT chest with contrast. As a general rule, soft tissue sarcomas will be T1 hypointense, T2 hyperintense, and contrast enhancing with variable amounts of non-contrast-enhancing necrosis. Additional studies are warranted in certain cases, including sarcomas with the potential for lymph node spread as summarized in the previously described pneumonic "RACES," for which a whole PET/CT is warranted. Myxoid liposarcomas require a whole-body MRI to evaluate for distant metastases which can occur in the bony spine or any soft tissue location.

If the disease is found to be isolated, the standard of care is radiation therapy before or after margin-negative surgical resection. Preop radiation increases the risk of wound healing complications, while postop radiation increases pain and fibrosis. Radiation can be avoided for lesions less than 5 cm and superficial lesions. The use of chemotherapy is dependent on the treating institution but is reliably used in the setting of metastatic disease and sensitive subtypes such as synovial sarcoma, alveolar rhabdomyosarcoma, and myxoid liposarcoma with a round cell component.

In a large series of non-metastatic disease, the rate of local recurrence of all extremity soft tissue sarcomas is 25% at 10 years with a disease-specific mortality of 40% at 10 years [61]. A positive margin at the time of resection will double the risk of local recurrence, while increasing pathologic grade, large size, and increasing age decrease overall survival [27, 61]. Metastases at presentation portend an overwhelmingly poor prognosis, with a 10-year survival rate of only 20% [61]. Other factors that negatively affect local recurrence and survival are an inadvertent excision requiring re-excision and tumor fungation, i.e., erosion of the skin overlying a sarcoma [63, 64].

Finally, postoperative surveillance should be carried out for 10 years after resection of a soft tissue sarcoma. The majority of local recurrences and development of metastases occur in the first 2 years; therefore, this regimen is most intense in the first 2 years and gradually decreases in frequency thereafter. It includes alternating local and chest XR with a local MRI and CT chest, starting at 3-month intervals.

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Part IV

Musculoskeletal Trauma and Rehabilitation

Systemic Response to Trauma

18

John J. Yoon, Elizabeth B. Dreesen,
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Contents

Goals and Objectives

- *Goals:* The purpose of this chapter is to introduce the reader to the human body's complex response to trauma. Recognizing the metabolic, biochemical, and physiologic responses will provide the reader with the necessary foundation to manage the critically injured patient.
- *Objectives:* By the end of the chapter, the learner should be able to:
  1. Evaluate and triage a trauma patient; list the correct sequence of the primary and secondary survey.
  2. Identify life-threatening conditions and apply the principles of initial resuscitation.

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3. Understand the physiologic effects of trauma and its global effect on the human body.
4. Recognize the clinical presentation of shock and understand the principles of managing the hypotensive patient.
5. Describe the alterations of metabolism in response to trauma and its clinical implications.

18.1 Introduction

The "tri-modal distribution of mortality" describes three phases in trauma during which injury causes death [1, 2]. The first peak in mortality occurs immediately after the traumatic event, caused by direct injuries to organs such as the brain, spinal cord, heart, and major blood vessels. The second peak occurs within hours following trauma. These patients arrive at the hospital alive, but they have experienced severe injury that progresses rapidly through uncontrollable hemorrhage or worsening hypoxia to death. The third peak, also known as late death, occurs days to weeks after the initial injury. Death in these patients is caused by sepsis and multi-organ failure.

All three peaks in the tri-modal distribution are closely intertwined, and it is critical to understand the constantly evolving condition of the trauma patient. The precious moments immediately after injury are known as the "golden hour" [3]. With proper care by specialized providers, this window of opportunity has the greatest impact on the patient's chance of survival. Survival rates do not decline after a precise 60 minutes, but the concept of the "golden hour" emphasizes the importance of prompt assessment and intervention. The goals of care should be minimizing the extent of trauma and preventing complications from injuries.

This chapter will introduce the systemic responses and the cascade effect that injury has on the human body. These responses are varied among patients and not always evident but they must be considered in the evaluation, resuscitation, and care of the trauma patient. Even localized injury has systemic ramifications and the clinician must understand these sequences to effectively care for them.

18.2 Evaluation of the Trauma Patient

A 36-year-old male presents to your trauma bay after sustaining a motorcycle accident. According to the emergency medical technician (EMT), he was wearing a helmet, but copious blood was visible at the scene. At quick glance, the patient has open deformities of his bilateral lower extremities with bruises and lacerations over both arms. His vital signs on arrival include a blood pressure (BP) of 83/43 and a pulse of 108.

18.2.1 The Advanced Trauma Life Support (ATLS) Protocol and Primary Survey

Clinicians must not only be decisive, but also systematic when managing the trauma patient. The combination of multiple visible injuries and the heightened sense of urgency among the staff members in the trauma bay can contribute to distraction. A traumatic accident can cause injuries well beyond the obvious ones in this case, and without focus, occult but critical injuries can be overlooked. For this reason the ATLS protocol was designed so that clinicians can quickly identify and treat life-threatening injuries first.

The primary survey is the initial evaluation once the patient arrives at the trauma bay. During this initial assessment, life-threatening injuries are assessed in sequence as in Table 18.1.

Determining *airway* patency is assessed by the patient's ability to communicate verbally. If the patient arrives from the field with an endotracheal tube already in place, a midline trachea and easy ventilation via bag valve mask (BVM) suggests an unobstructed airway. *Breathing* is the second step of the primary survey. An unobstructed airway does not definitively confirm adequate gas exchange at the level of the lungs. Auscultation of the lungs indicates whether gas is entering the thoracic cavity and expanding the

Table 18.1 The ABCs of the primary survey (From ATLS Student Course Manual) [2]

A	Airway maintenance with restriction of cervical spine motion
B	Breathing and ventilation
C	Circulation and hemorrhage control
D	Disability (assessment of neurologic status)
E	Exposure/environmental control

Table 18.2 Glasgow Coma Scale

Eye opening	Verbal response	Motor response
4 – Spontaneous opening	5 – Oriented	6 – Follows commands
3 – Opens to command	4 – Confused	5 – Localizes pain
2 – Opens to pain	3 – Inappropriate words	4 – Withdraws from pain
1 – No response	2 – Incomprehensible sounds	3 – Flexion with pain
	1 – No response	2 – Extension with pain
		1 – No response

lungs. *Circulation* is evaluated by palpating peripheral pulses and checking a blood pressure. Hemorrhage – obvious or occult – and injuries to major blood vessels must be ruled out in this step of the assessment. Next, *disability* assesses neurologic function and level of cognition in a patient with potential brain injury. The Glasgow Coma Scale (GCS) tests cognitive function by assessing eye movement, verbal response, and motor function (Table 18.2). Lastly, *exposure* is performed by completely undressing the patient to allow for a thorough physical examination and identification of other injuries.

18.2.2 Acute Resuscitation

Signs of compromise identified during the primary survey must be promptly addressed as soon as they are noted. The ATLS protocol was designed so that the most life-threatening injuries are assessed and treated before attending to other injuries. Open fractures, deep wounds, and obvious deformities can be distracting but the key to evaluating a trauma patient is assessing the "ABCs" in an organized fashion.

Airway – A patient who is unable to speak clearly with audible stridor or blood or vomitus in the airway requires an immediate definitive airway. Oropharyngeal foreign bodies, facial bone fractures, tracheal injury, and altered mental status are common causes of airway obstruction. In severe obstruction where endotracheal intubation is not possible, one must consider a surgical airway (i.e., cricothyrotomy, tracheostomy). Maintaining a midline cervical spine while examining and controlling the airway is also critical, as excessive mobilization of the neck can exacerbate spinal cord injury. Placement of a cervical collar is performed in this step.

Breathing – Injuries to the chest wall can lead to a pneumothorax, hemothorax, and bronchial injury. Decreased breath sounds, oxygen desaturation, and unequal chest rise require insertion of a thoracostomy tube. Without proper diagnosis, addition of positive pressure in the thorax can lead to a tension pneumothorax resulting in circulatory collapse.

Circulation – A patient presenting with circulatory compromise is hypotensive, tachycardic, and diaphoretic and may have waxing and waning consciousness. Although these symptoms can be associated with other injuries, the clinician must eliminate hemorrhage as a cause. There are six compartments in the body where blood can accumulate: chest, abdomen, long bones (femurs), pelvis, retroperitoneum, and "street" (blood lost at the scene of injury) [3]. In the hypotensive patient, the FAST (focused assessment with sonography for trauma) utilizes the ultrasound to look for blood accumulating in the pericardium, hepatorenal space, splenorenal space, and pelvis. Once circulatory compromise is identified, intravenous access must be obtained and restoration of blood volume must be immediately initiated while also identifying the source of bleeding. Many times, obvious external bleeding can be controlled with direct digital pressure, application of tourniquet, pelvic binder, or extremity splints [4]. Ultimately, definite hemorrhage control is paramount and patients who

remain hypotensive require an emergent operation.

Disability –Drugs, intoxication, and other medical problems can all contribute to altered consciousness, but the goal of this step is identifying traumatic brain injury. The GCS has a maximum score of 15 and a minimum of 3. Patients with GCS of 8 or below are deemed too altered to protect their airway and require orotracheal intubation. In addition to the GCS, assessments of pupillary size, pupillary reaction to light, and movement of all four extremities are used to identify neurologic injury during the primary survey. A fixed, unilateral, and dilated pupil in patients suggests an intracranial bleed that requires an emergent neurosurgical evaluation.

Exposure – All clothes and undergarments must be removed from the patient. The whole body must be exposed to identify all associated injuries. Especially in penetrating trauma, injuries can be hidden in the axillae, perineum, and back. After fully exposing the patient, warm blankets or other external heating devices are applied to prevent hypothermia which is the sequelae of resuscitation in a cold environment with cold fluids. All intravenous fluid should be warmed prior to administration and the trauma bay should be maintained at a warm temperature.

The primary survey – with its organized steps of assessment and treatment – should be completed rapidly. Each step is designed to prevent early death. However, an efficient primary survey with early and appropriate treatment of life-threatening shock and hypoxia also minimizes the metabolic and physiologic stress that is discussed below and which is associated with complications including coagulopathy, sepsis, and multi-organ failure.

The secondary survey follows the primary survey and serves to identify further injuries. This evaluation includes a complete history and a thorough physical examination. This assessment is a key component in the identification of all injuries including fractures and soft tissue injury. Even injuries that are not associated with life-threatening shock can set off systemic responses associated with increased risk of complication in the post-injury period.

18.3 Shock in Trauma Patients

Shock is the state of low blood flow that results in decreased perfusion and oxygenation of the tissues [2, 5]. When the supply of oxygen fails to keep up with the metabolic demands, a number of systemic responses are initiated. Though trauma patients with shock most commonly present with hemorrhagic shock, distributive (tension pneumothorax), cardiogenic, and neurogenic shock can also be present in trauma patients. Compromised organ perfusion is nonetheless a feature of all shock in trauma patients.

The physiology of shock can be best understood by cardiac output (CO) equation [2, 5]. Cardiac output is the volume of blood the heart pumps throughout the body in one minute. In an average healthy adult, this is approximately 5 L/min.

$$\mathrm{CO} = \text{Heart rate}\left(\mathrm{HR}\right) \times \text{Stroke volume}\left(\mathrm{SV}\right)$$

CO is the product of heart rate (HR) and stroke volume (SV). SV is the volume of blood ejected by the left ventricle during one cardiac cycle. SV is influenced by three factors: the volume of blood returning to the heart (preload), the pressure the heart must work against to eject blood (afterload), and the inherent strength of the cardiac muscle fibers to contract (contractility) [2]. With blood loss, the body compensates for the decrease in CO by increasing in HR via the adreno-sympathetic pathway. This same pathway causes an increase in peripheral vascular resistance (PVR) to maintain a normal blood pressure. Therefore, a trauma patient who presents with tachycardia should be treated with high level of suspicion for hemorrhagic shock. Though pain, anxiety, and substance ingestion can also cause tachycardia, the severely injured patient is presumed to have tachycardia from shock until careful evaluation reveals otherwise.

18.3.1 Hemorrhagic Shock

Blood pressure readings can quickly and accurately monitor hemodynamic status, but other clinical signs of hypovolemia should be quickly sought in the trauma patient. This is especially true in younger patients who are able to compensate for blood loss with tachycardia and vasoconstriction more effectively than do their older counterparts.

With hemorrhagic shock there is an increase in peripheral vascular resistance (PVR), which leads to an increase in systolic blood pressure and a reduced pulse pressure. Clues to shock despite normal systolic blood pressure include cool, clammy skin and decreased capillary refill which occur secondary to sustained vasoconstriction of the skin. The lack of oxygen delivery and perfusion prompts increasing anaerobic metabolism and tachypnea to compensate for metabolic acidosis. Decreased urine output is also the result of inadequate blood flow to the kidneys. The degree of blood loss can be correlated with the severity of these symptoms and clinical observations. The classification of hemorrhage categorizes blood loss into four categories and the spectrum of symptoms associated with the amount of blood loss (Table 18.3).

18.3.2 Transfusion and Coagulopathy

One of the major methods of treating hemorrhagic shock is replacing the lost blood volume with intravenous fluid. In order to accomplish this, intravenous access must be obtained with bilateral large-bore intravenous catheters [2]. Although saline has traditionally been used for initial resuscitation, earlier use of blood products has shown to improve survival [6], while administration of more than 1.5 L of crystalloids has been associated with mortality [7]. Patients who require blood immediately during their resuscitation are given O-negative red blood cells (pRBCs) until fully cross-matched blood is available. Patients who do not respond to the initial resuscitation must be suspected of ongoing hemorrhage and may require multiple consecutive transfusions of blood products. The wars in Iraq and Afghanistan have prompted deep investigation into hemorrhagic shock and transfusion of blood products. Current recommendations for patients who require multiple blood products include minimizing crystalloids and administering pRBCs, plasma, and platelets in a balanced ratio [2].

Multiple transfusions, however, are not without complications. Circulatory overload and pulmonary edema (known as TACO or transfusion-associated circulatory overload) may develop in the multiply transfused trauma patient. TRALI (transfusion-related acute lung injury), an immune-mediated form of non-cardiogenic pulmonary edema resulting from donor antibodies, may also occur [8, 9]. In the longer term, transfusion has been associated with immunosuppression and increased risk of infection in the post-trauma period [10]. These transfusion-related complications should

Table 18.3 Signs and symptoms of hemorrhage by class [1]

Parameter	Class I	Class II	Class III (moderate)	Class IV (severe)
Approximate blood loss	<15%	15–30%	31–40%	>40%
Heart rate	⟷	⟷/↑	↑	↑/↑↑
Blood pressure	⟷	⟷	⟷/↓	↓
Pulse pressure	⟷	↓	↓	↓
Respiratory rate	⟷	⟷	⟷/↑	↑
Urine output	⟷	⟷	↓	↓↓
Glasgow Coma Scale score	⟷	⟷	↓	↓
Base deficit[a]	0 to −2 mEq/L	−2 to −6 mEq/L	−6 to −10 mEq/L	−10 mEq/L or less
Need for blood products	Monitor	Possible	Yes	Massive transfusion protocol

Data from: Mutschler et al. [28]

[a]Base excess is the quantity of base (HCO_3^-, in mEq/L) that is above or below the normal range in the body. A negative number is called a base deficit and indicates metabolic acidosis

highlight the importance of early control of hemorrhagic shock.

The clinician must also consider the development of coagulopathy. Receiving numerous crystalloid boluses and pRBCs leads to the dilution of coagulation factors. In addition, hypovolemic states shift fluid lacking in coagulation factors from the interstitial space to the intravascular space [11]. While dilutional and consumptive coagulopathy have long been the focus of attention in traumatic coagulopathy, new research in "acute trauma coagulopathy" implicates activation of protein C activity with inflammation, destruction of endothelium, and activation of platelets as a source of coagulopathy that occurs even before transfusion [12].

Without careful attention to urgent hemorrhage control and the details of transfusion, multiple transfusions can be associated with hypothermia, worsening acidosis, and electrolytic abnormalities including hyperkalemia and hypocalcemia. In fact, the "lethal triad" of trauma coagulopathy is well known to trauma surgeons and includes hypothermia, continued coagulopathy, and acidosis [13]. Each component synergestically impairs the other components, forcing the patient into a vicious cycle associated with high morbidity and mortality. Trauma patients in shock can be profoundly hypothermic from multiple factors: under-perfused skeletal muscles, inability to shiver, prolonged exposure to the environment, and transfusion of non-warmed saline. Acidosis is caused by the formation of lactic acid from poor perfusion and tissues undergoing anaerobic metabolism. The combination of low temperatures and acidosis severely impairs coagulation factors, worsening the coagulopathy. The use of warming devices and warmed saline during an operation is imperative during acute resuscitation [13].

18.4 Physiologic Response to Trauma

We have focused above on shock and traumatic injuries that immediately threaten life. However, *all* trauma – not just life-threatening trauma – prompts an immediate host response to injury that is highly dependent on the immune system. At the cellular level, there are a series of reactions that ignite the healing. While cell signaling can be initiated at a localized level, injury prompts systemic response as well, even in less injured patients. Both local and systemic responses to localized trauma have significant impact on the treatment and outcome of injury.

18.4.1 The Acute Inflammatory Response

The acute inflammatory process is initiated when tissue damage is recognized by circulating neutrophils [14]. Recent studies show that neutrophils detect damage-associated molecular patterns (DAMPs) which are proteins released endogenously in response to tissue injury [15]. Neutrophils then tightly bind to the exposed endothelium via cell adhesion molecules. These cells are known for their ability to release lytic enzymes and remove dead tissue by phagocytosis, but they play an important role activating the immune system by the release of cytokines, cell signaling molecules that recruit other cells and activate the immune system. There are many different types of cytokines and their roles range from inducing differentiation of immunologically active cells to propagating both pro-inflammatory and anti-inflammatory cascades.

Platelets are also early mediators of inflammation. They are the first cells to arrive at the site of injury and their roles are also initiated by binding to the endothelium. Although platelets are known for their role in hemostasis, the release of prostacyclins, thromboxanes, and platelet-derived growth factors (PDGFs) serves a unique function in cell communication and recruitment. Platelets also recruit fibroblasts which lay the framework for wound healing [5].

Macrophages are also heavily involved in the acute inflammatory process. They also remove debris by phagocytosis, but release two very important cytokines: TNF-ß and IL-1 [16]. These two cytokines have very strong and widespread effects on the body. They work synergistically to increase molecules for adhesion, activate more

Table 18.4 Symptoms of systemic inflammatory response syndrome

Temperature	>38° or < 36 °C
Heart rate	>90 beats/minute
Respiratory rate	20 breaths/min or PaCO2 < 32
White blood count	>12,000/⌠L or < 4000/⌠L

immune cells, and induce fever. TNF-ß specifically has even been shown to cause cachexia, circulatory collapse, and ultimately multisystem organ failure. Production of IL-1 leads to vasodilation, hypotension, and increased pain sensitivity [5, 17].

The cascade of these localized cellular responses, if amplified sufficiently, can result in a familiar set of symptoms known as the systemic inflammatory response syndrome (SIRS) (Table 18.4). This involves multiple organ systems and affects all body parts. By definition, a patient is manifesting a SIRS when he or she has two or more of the following [18–20].

Patients with SIRS must be identified early and require close monitoring as the SIRS response can progress to more morbid conditions such as acute respiratory distress syndrome (ARDS) and multi-organ dysfunction syndrome (MODS) [17].

18.4.2 Neuroendocrine Activation

The neuroendocrine system activates the sympathetic autonomic system and stimulates pituitary hormone release [21, 22]. The hypothalamus is the primary mediator of the neuroendocrine response and is activated by pain, hypovolemia, and inflammation. At the site of injury, pain is sensed by the unmyelinated C and myelinated A fibers. These pain signals reach the hypothalamus via the spinothalamic tract. Hypovolemia on the other hand is detected by the baroreceptors in the carotid bodies and the atria of the heart. They reach the hypothalamus via cranial nerves IX and X. Inflammation and the release of cytokines have localized effects but also have great roles in modulating the neuroendocrine system [22, 23].

Activation of the sympathetic system delivers a powerful "fight or flight" response by releasing norepinephrine and epinephrine. Their effects are immediate and frequently short lived, but can be prolonged by severe injury. They induce the multiple alpha and beta adrenergic receptors in the body, resulting in hypertension, increased cardiac output, and energy mobilization. Renin is released by the kidneys and activates the renin-angiotensin system which stimulates sodium reabsorption to increase the intravascular volume. Glucagon is also released in the pancreas which promotes glycolysis and gluconeogenesis [5, 23, 24].

The endocrine effects from the pituitary gland complement the sympathetic system response by regulating substrate metabolism and fluid balance [21, 24]. The hypothalamic-pituitary-adrenal (HPA) axis works through complex feedback mechanisms to release cortisol, an important hormone with multiple roles in the stress response. Cortisol promotes lipolysis and proteolysis to provide gluconeogenic substrates. It also has mild anti-inflammatory properties, inhibiting neutrophils and macrophages from accumulating in the areas of inflammation [25]. It also stimulates the reabsorption of sodium in the intestines, thereby increasing the intravascular volume.

Other important pituitary hormones are growth hormone (GH) and antidiuretic hormone (ADH). ADH is produced in the hypothalamus and released by the posterior pituitary gland. ADH has multiple roles but in the stress response works on the kidneys to increase water reabsorption in the collecting tubules. Growth hormone is also secreted by the posterior pituitary gland and promotes lipolysis and gluconeogenesis [5]. The major hormones involved in the neuroendocrine response are summarized in Table 18.5.

18.5 Metabolism and Nutrition

The systemic response to injury imposes a large metabolic burden. In fact, the stress of trauma can increase the metabolic rate up to 25–30% [26]. This is most evident in burn patients and patients with traumatic brain injury, though multi-system trauma of all sorts is associated with some degree of hypermetabolic state. This

Table 18.5 Hormones involved in the acute injury response

Cortisol	Steroid hormone that increases blood sugar through gluconeogenesis. Can lead to muscle protein breakdown. Mild effect on sodium abosrption; mild antiinflammatory properties
Renin	Released in response to decreased blood flow to kidneys. Converts angiotensin I to angiotensin II. Angiotensin II is a powerful vasoconstrictor and releases antidiuretic hormone and aldosterone
Aldosterone	Mineralocorticoid hormone released from the adrenal cortex. Stimulated by renin production. Potent effects on kidneys resulting in sodium reabsorption and water retention
Antidiuretic hormone (ADH)	Produced in the hypothalamus and released by the posterior pituitary gland. Works on the kidneys to retain water, also a potent vasopressor. Release is also enhanced by ACTH
Growth hormone	Secreted by the anterior pituitary gland. Facilitates glycogenolysis and lipolysis for the production of glucose
Glucagon	Released by the alpha cells of the pancreas to increase blood glucose. Stimulated by epinephrine

state can be quite prolonged depending on both injury and the development of post-injury complications (including especially infectious complications) which can reactivate the post-trauma hypermetabolic state.

18.5.1 Metabolic Changes in the Trauma Patient

The metabolic response to trauma has been described as having three phases: ebb, flow, and anabolic. The ebb is the sudden decrease in metabolic rate, beginning from the onset of trauma to the first 48 hours in which metabolism slows to adjust to the change in tissue perfusion associated with shock. The flow phase, which occurs during the days to weeks after injury, is characterized by hypermetabolism and the rapid breakdown of energy stores to provide substrates for the "fight or flight" reactions to infections and other complications. The anabolic phase occurs weeks to months after the trauma when the body restores and rebuilds its body tissues [23, 26].

With shock and inadequate perfusion associated with injury, glucose becomes the primary source of energy. Glucose produces 4 kcal/g and has the ability to be utilized in hypoxic tissues through anaerobic metabolism. During acute inflammation, immune cells such as neutrophils and macrophages are heavily reliant on glucoses' ability to be anaerobically metabolized. This glucose initially comes from glycogen stores in the liver which are rapidly broken down and last up to 24 hours. Once glycogen is depleted, glucose is produced from lactate and amino acids that come from catabolism of lean muscle mass. A common complication of rapid glucose mobilization during trauma is hyperglycemia. In the non-injured state, insulin modulates glucose levels by creation of glycogen and fat. However, when the body reacts to injury, the release of catecholamines and neuroendocrine hormones creates a state of insulin insensitivity and raises the blood glucose level [24, 26].

Both the ebb and flow phases are heavily dependent on the metabolism of fats as they are the ideal sources of energy. Fats are abundant in the body, are broken down easily, and provide the most energy: 9 kcal/g. Fatty metabolism is accelerated by the release of catecholamines and the hormones involved in the neuroendocrine response. Triglycerides are broken down to fatty acids and glycerol. Glycerol is an important substrate for gluconeogenesis in the liver, while fatty acids are oxidized in the liver to produce energy [21, 26, 27]. Triglycerides provide 50–80% of total energy consumption in stressed states [26].

Proteins are also broken down with trauma which results in muscle wasting. Skeletal muscles are a prime source of alanine, an essential amino acid substrate for gluconeogenesis. Other branched chain amino acids (BCAA) like glutamine can only be used in injured tissues. Amino acids are also important for wound healing, protein synthesis, and immunologic function. Amino acids are the building blocks of albumin, fibrinogen, acute phase proteins, and complement factors. Prolonged injury without protein supplementation can lead to a loss of up to 1 kg

of lean body mass per day as the stress response leads to the breakdown of the body's muscle in order to supply the amino acids required for gluconeogenesis and new protein synthesis [5, 26].

18.5.2 Nutritional Support

When the body undergoes an all-or-nothing response to injury and amplifies the metabolic process, nutritional supplementation becomes critical. The goal is to minimize the catabolic impact of the hypermetabolic response and supply the body with substrates to prevent further breakdown of the injured patient's tissues. Although the anabolic phase of metabolism occurs weeks after a long recovery from the ebb and flow phases, early initiation of nutrition can prevent malnutrition, decrease the amount of catabolism that weakens the injured patient, and counterbalance the metabolic load of trauma [27].

The basal energy expenditure (BEE) can be calculated by the Harris-Benedict equation. Males tend to have a higher basal energy expenditure due to greater lean body mass [5]. *W* is weight in kg, *H* is height in cm, and *A* is age in years.

$$\text{Male BEE} = 66 + (13.7 \times W) + (5.0 \times H) - (6.8 \times A)\,\text{kcal/d}$$
$$\text{Female BEE} = 655 + (9.6 \times W) + (1.85 \times H) - (4.7 \times A)\,\text{kcal/d}$$

Patients who sustain severe trauma will have an increased BEE of 25% to 50% above baseline, approximately 30 kcal/kg/day. In addition to the increased caloric demand, adequate protein intake is necessary for the preservation of lean muscle mass. Protein is an important resource for wound healing and immunologic function. The ratio of non-protein calorie/nitrogen should be 100:1 or 150:1 to limit the use of protein as an energy source (6.25 g of protein = 1 g of nitrogen). While the average patient receives 1 g/kg of protein, trauma patients should receive 1.25 g/kg of protein [27].

18.5.3 Final Word

The body deploys numerous defenses in response to traumatic injury. In the face of trauma, neuroendocrine, biochemical, immunologic, and physiologic pathways are activated in an immediate attempt to limit the threat to life and subsequently to restore the body to its pre-injury state. Although these responses are immediately beneficial, prolonged activation of these pathways can be detrimental. Prolonged pro-inflammatory state can be associated with ARDS and acute renal failure. Protracted hypermetabolism and catabolism lead to loss of lean muscle mass and weakening of both anatomic and immunologic defenses.

Effective and efficient care during the "golden hour" can identify and limit the damage done by trauma and the ensuing tissue injury and hemorrhage. This, however, is not sufficient to ensure good outcomes after injury. Attentive and thorough postoperative care is required to prevent iatrogenic complications that prolong or reactivate the stress response. Pulmonary toilet to prevent pneumonia, minimization of device-associated infection, early and adequate nutritional support, and early mobilization are also critical components of trauma care, enabling the body to transition early to the anabolic phase of recovery.

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19 Principles of Musculoskeletal Fracture Care

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Contents

Goals and Objectives

- *Goal:* To introduce the reader to the general principles of musculoskeletal fracture care, which include both operative and nonoperative management.
- *Objectives:* On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe, list, or identify the:

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1. Forces acting on bones that can result in a fracture
2. Initial ED management, workup, and diagnosis of fractures
3. Descriptive terminology of fracture radiographs and the Gustilo-Anderson classification of open fractures
4. Appropriate emergency department management of open fractures
5. Clinical diagnosis of compartment syndrome
6. Nonoperative treatment options for management of fractures
7. Operative treatment options for management of fractures
8. Definition of absolute and relative fracture stability and the effect on bone healing
9. Unique characteristics of pediatric fractures
10. Common complications of musculoskeletal fracture care

19.1 Introduction

Fractures are a common cause for emergency room visits in the United States, affecting both children and adults. More than 50% of hospitalized trauma patients have a musculoskeletal injury that can result in significant functional impairment [1]. Age-related fractures, due to *osteopenia* or *osteoporosis*, are estimated to approach 3 million fractures by 2025 [2]. The primary goal of fracture care is to ensure the injured extremity is returned to its full function. This can be achieved by operative or nonoperative means, depending on the fracture type. Having a basic knowledge in the diagnosis and management of fractures can significantly decrease patient morbidity and mortality.

19.2 Etiology

Bone is an organ that (1) protects soft tissue structures in the body, (2) allows for ambulation, and (3) allows mechanical functioning of extremities [3]. A *fracture,* or *broken bone*, occurs when the force exerted on a bone is greater than the strength of the bone itself [3, 4] . This can occur from a single event or due to repetitive overload in the case of a *stress fracture.* Fractures can occur from both high- and low-energy mechanisms. Examples of high-energy mechanisms include gunshot injuries, motor vehicle collisions, or falls from heights. An example of a low-energy mechanism is a fall from standing [4]. Whether a patient sustains a fracture is based on several factors, including the quality of the bone and the amount and direction of force applied to the bone. Osteoporotic changes due to aging can significantly alter the amount of force required to cause a fracture [5]. For example, a 24-year-old medical student is less likely to sustain a hip fracture after a slip and fall than a frail 80-year-old woman with osteoporosis.

There are several forces that can act on bone: compression, torsion, tension, and bending. When these forces are great enough to cause the bone to fracture, it will lead to predictable fracture patterns that can be identified on radiographs [4]. A *transverse fracture* (Fig. 19.1a) is typically due to a tension force and is identified on a radiograph with a fracture line that is perpendicular to the long axis of the bone. An *oblique fracture* (Fig. 19.1b) is often due to a compressive force. A bending force will often cause a transverse fracture on the tension side of the bone and comminution, or a butterfly fragment, on the compression side of the bone (Fig. 19.1c). Higher-energy forces lead to *comminution*, or fragmentation of the bone into more than two fragments (Fig. 19.1d). The degree of comminution often indicates higher-energy mechanisms. Torsional, or twisting, forces will typically cause a classic *spiral fracture pattern* (Fig. 19.1e) [4]. *A*

segmental fracture is one where the bone has more than one fracture line, often resulting in a "segment" of bone in the center.

19.3 Presentation and Diagnosis

Upon presentation to the emergency room or clinic, a thorough history should be taken, emphasizing the events or activity leading up to the injury. Comorbidities and medications should be reviewed. Bisphosphonates, which are used to treat osteoporosis, can occasionally lead to atypical fractures [6, 7]. As we saw in the previous section, forces applied to bones can lead to predictable fracture patterns. This is helpful in determining initial therapy, since reduction and stabilization of the fracture depends on a reversal of the deforming or injuring forces. If no life-threatening injuries have been identified (following ABCDEs), a targeted musculoskeletal exam can be performed on the involved limb. Skin should be meticulously inspected for evidence of an *open fracture*. Neurovascular status should be carefully evaluated, including distal pulses and sensation and motor exam. Failure to timely identify a vascular or neurologic deficit can result in devastating complications, including loss of limb or function. X-rays should be obtained of the entire bone suspected to be injured, including the joints above and below. *Orthogonal*, or two views that are 90 degrees to one another (i.e., AP and lateral), should be obtained, at a minimum. Additional radiographic views, such as oblique X-rays or *stress radiographs*, can be obtained later, depending on the injury pattern. For more

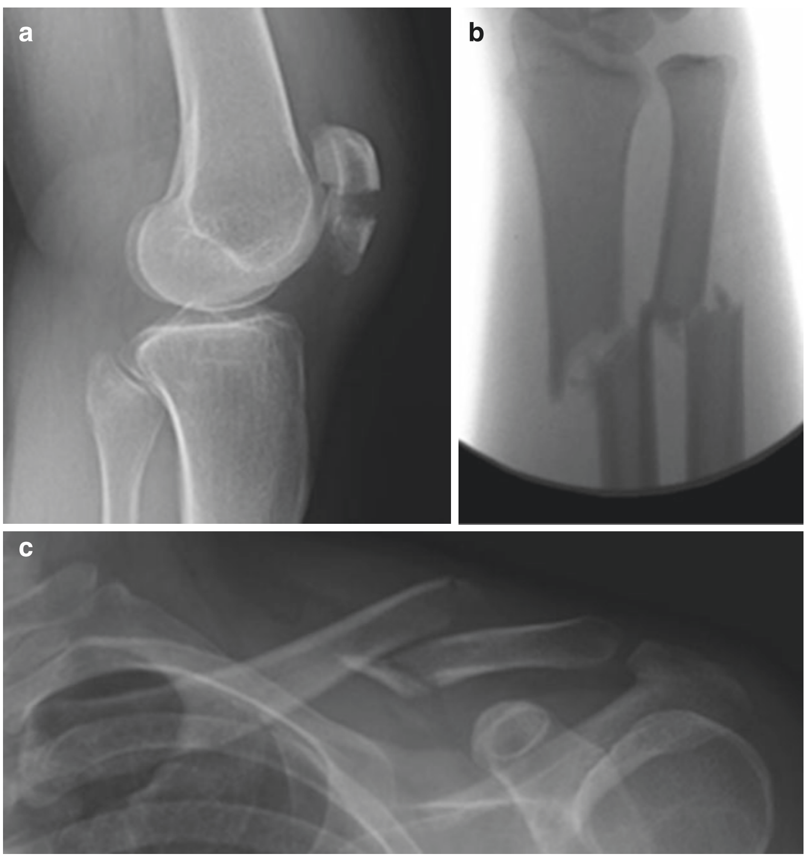

Fig. 19.1 (**a**) Lateral X-ray of knee showing transverse fracture of the patella. (**b**) AP image of an oblique fracture of the radius and ulnar shafts. (**c**) AP X-ray of a clavicle fracture showing a butterfly fragment. (**d**) Severely comminuted fracture of the proximal humerus. (**e**) Spiral fracture of the tibial shaft

Fig. 19.1 (continued)

complex fractures, such as *intraarticular fractures*, computerized axial tomography (CAT) scan may be ordered to aid in surgical planning.

19.4 Description and Classification of Fractures

There is essential descriptive terminology that should be used when describing a fracture on a radiograph. This includes the anatomic location, bone involved, fracture pattern (described in the previous section), morphology of the fracture, and the direction of displacement. *Fracture displacement* is the position of the distal fracture segment in relation to the proximal segment. A nondisplaced fracture has no displacement and is in anatomic position. A displaced fracture may be described based on its angulation, translation, and rotation of distraction/impaction. An *intraarticular fracture* is one that involves the joint surface and deserves special consideration. Intraarticular fractures require an anatomic reduction, usually by open reduction techniques (i.e., surgery) to reduce the risk of traumatic arthritis and future pain. For example, in Fig. 19.2 the fracture can be described as follows: a diaphyseal, transverse femur fracture with medial translation and shortening. A *periprosthetic fracture* is a fracture that occurs at or around an orthopedic implant, such as a total hip or knee replacement. *A pathologic fracture* often occurs after a low-energy mechanism and is a result of an underlying process that weakens the mechanical strength of the bone, such as a severe

Fig. 19.2 AP radiograph showing a transverse femur fracture

osteoporosis, bone cysts, tumors, or other lytic lesions.

Clinically, it is also important to note whether the fracture is open or closed, or if there is any evidence of threatened skin (bone tenting skin). A *simple, or closed, fracture* is a fracture within its soft tissue envelope and does not communicate with the exterior environment. *An open, or compound, fracture* occurs when a fracture fragment or fracture hematoma communicates with the outside environment (i.e., breaks through the skin).

19.5 Management of Open Fractures

Open, or compound, fractures require special attention due to their increased complexity and associated morbidity. Open fractures are typically the result of high-energy trauma, where the fractured bone penetrates through the skin. When the body's protective skin layer is broken, exposing a fracture to the outside environment, the potential for contamination and resultant infection are significantly increased. *Osteomyelitis* is a rare, but serious condition that involves an infection of the bone. Additionally, associated soft tissue injury, periosteal stripping, and disruption of the local blood supply at the fracture may increase the risk of *nonunion or delayed union*. *Nonunion* is a radiographic diagnosis characterized by failure of bone trabeculae to bridge the fracture site.

Open fractures are often associated with the application of a violent force to an extremity. Energy transmitted after a fall from a curb has been estimated at 100 ft-lb. This is compared to a 20-mph motor vehicle collision, which can transmit energy transmitted up to 100,000 ft/lb [8]. In the emergency department, all open cuts or wounds on the skin should be thoroughly inspected to determine if they are associated with a fracture. Any wound occurring around a fracture should be considered an open fracture until proven otherwise [8]. Open fractures are most commonly classified using the Gustilo-Anderson classification system (Table 19.1) [9]. Like closed fractures, open fractures are initially treated with closed reduction and splinting. However, prior to splinting, open wounds should be thoroughly irrigated with normal saline, and a sterile dressing should be applied until the patient arrives in the operating room. Additionally, human tetanus antitoxin (if not up to date) and antibiotics should be promptly administered. Antibiotics should

Table 19.1 Gustilo and Anderson open fracture classification [9]

Type 1	Clean wound measuring less than 1 cm
Type 2	Skin laceration >1 cm but less than 10 cm, with minimal contamination and/or nonviable tissue
Type 3a	Extensive soft tissue damage >10 cm in size, with or without significant wound contamination
Type 3b	Like type 3a, but such extensive soft tissue injury that it requires soft tissue coverage such as a flap
Type 3c	Open fracture with associated arterial injury that requires vascular surgery repair

preferably be given within 1 hour of the inciting event or as soon as possible. For type 1 and 2 open fractures, a first-generation cephalosporin is typically administered. For type 3 open fractures and other high-energy fractures, additional antibiotics, historically an aminoglycoside, are typically recommended to cover gram-negative flora. If there is high suspicion for a farm-related injury, IV penicillin is added to the regimen to cover for possible wound contamination with *Clostridium* species [8].

A patient's risk of developing an infection after an open fracture depends on several factors, including fracture location, fracture severity, timing to antibiotic administration, and time to operative management. Studies have shown that the most common complication after type 3 open tibia fractures is wound infection. Prompt administration of antibiotics and emergent irrigation and debridement of open fractures leads to a decreased risk of infection. The literature is controversial on the timing to the operating room but the higher-grade injuries (Gustilo type 3) should be taken immediately for operative irrigation and debridement or as soon as the patient is medically stable. Lower-grade injuries (Gustilo types 1 and 2) can be done in an urgent fashion the following morning if necessary [10–13].

19.6 Treatment

19.6.1 Closed Reduction

Followed by a thorough history, physical exam, and radiographs, the primary goals of fracture management in the emergency department are closed reduction and immobilization. *Closed reduction* is the "re-alignment" of a fracture by manipulation only. Unless contraindicated, displaced fractures that will likely require surgery should still undergo attempted closed reduction, especially if the fracture is severely displaced or angulated and threatening the skin. Closed reduction requires understanding of the mechanism of injury and deforming forces that are contributing to fracture displacement. Closed reduction is performed with manual traction and *reversal of the injuring forces* to correct the length, rotation, and angulation of the fracture [14].

Urgent closed reduction of fractures has several clinical benefits in the acute setting, including (1) minimizing soft tissue trauma, (2) providing pain control, (3) decreasing potential space for bleeding, and (4) relieving threatened skin or impinged nerves and blood vessels. Often, severely displaced fractures, especially in the lower leg or ankle, may have diminished or absent pulses at presentation that will improve following a closed reduction. Fractures with no displacement do not require a closed reduction, but typically do require immobilization in a splint or a cast to prevent future displacement. Severely comminuted fractures or fractures that are unable to be reduced and immobilized in a splint or a cast (e.g., clavicle or patellar fractures) do not require a closed reduction.

19.6.2 Compartment Syndrome

Acute compartment syndrome remains a well-recognized orthopedic emergency that can lead to potential devastating complications for patients [15]. Contractures, insensate limbs, and even amputation represent some of the devastating sequelae of missed or delayed diagnosis of compartment syndrome. There are several causes of acute compartment syndrome, with orthopedic trauma being the most common. Muscles in the upper and lower extremity are confined to fascial compartments. For example, in the lower leg, the musculature is divided into four compartments, consisting of anterior, lateral, superficial, and deep posterior. Acute compartment syndrome develops when pressure in a muscle compartment increases to a critical threshold, resulting in decreased muscle perfusion and capillary collapse. Capillary collapse results in muscle ischemia and, eventually, necrosis [16]. The most common locations to develop compartment syndrome are in the lower leg after tibia fractures, followed by the forearm. A high index of suspicion is usually required to make a prompt diagnosis. In the awake and alert patient, severe, worsening pain despite adequate analgesia and

swollen, firm compartments should lead physicians to consider a clinical diagnosis of impending compartment syndrome. Pain on passive stretch and decreased sensation are the earliest clinical signs of compartment syndrome due to occlusion of small blood vessels supplying the muscle and nerves. Paralysis and pulselessness should never be used in the diagnosis of acute compartment syndrome. These are typically late manifestations of a *missed compartment syndrome* where muscle and nerve damage may already be irreversible. Patients who are unable to cooperate with a physical exam (i.e., obtunded, intubated, or sedated) pose a challenging diagnostic dilemma. In these patients, manual compartmental pressure monitoring should be utilized. This is achieved with a commercially available needle pressure device. Both absolute compartment pressures above 30 mmHg and a pressure differential (diastolic blood pressure – the measured compartment pressure, often referred to as delta P) of less than 30 mmHg are used to make the diagnosis. Once the diagnosis of acute compartment syndrome is made, the treatment is an emergent fasciotomy, or surgical release of the fascial compartments, to allow for reperfusion to the extremity [15–19].

19.6.3 Nonoperative Treatment of Fractures

Following closed reduction of a fracture, now (hopefully) in near anatomic alignment, the goal of treatment is to maintain the reduction by internal or external fixation (operative) or by closed, nonoperative methods. Nonoperative management consists of closed reduction maintenance of fracture alignment with a cast or a splint for 6–12 weeks, depending on the fracture. For most adult fractures, splinting is the preferred method of fracture immobilization in the acute setting, which allows for swelling in the days following the injury. Splints may be prefabricated or custom made [14]. Plaster is typically the preferred material for splinting as it is more pliable and slower setting than fiberglass (used more often in casting), which allows more time to mold the splint. The type of splint applied depends on the location of the injury and the mold required to maintain the reduction. Some general principles of splinting include immobilizing the joint above and below to control for rotation and "three-point contact" mold, which is required to maintain most reductions. Most upper extremity fractures involving the forearm or wrist can be maintained with a *sugar tong splint*. In a sugar tong splint, a U-shaped plaster slab is applied to the volar and dorsal aspects of the forearm, wrapping around the elbow [14, 20, 21].

A short leg splint is applied for most foot and ankle fractures. The extremity is well-padded with cotton roll, and a posterior plaster slab is applied from the toes to just below the knee crease and another U-slab is applied from medial and lateral around the malleoli. For fractures of the tibial shaft or about the knee, a short leg splint can be advanced to a long leg splint by extending the plaster proximal to the knee joint to the mid-thigh [14, 20, 21].

Casts remain the most common method of fracture treatment throughout the world. They are applied by wrapping plaster or fiberglass around an extremity that has been padded with synthetic wool or cotton. Again, a full cast is not usually applied immediately after an adult fracture due to the potential for swelling [14].

19.6.4 Traction

Traction is a basic treatment principle of orthopedics. Traction involves a steady, pulling force which is used to reduce a fracture. Today, due to the advances in orthopedic implants in the United States and other developed nations, traction is rarely used for definitive management of fractures. Instead, it is most often utilized as a temporalizing measure until definitive fixation can be performed. Traction will facilitate fracture reductions by restoring length and general alignment and provide patients with pain relief by relieving muscle spasm as well as tamponade bleeding vessels. There are two modalities of mechanical traction: skin traction and skeletal traction. In skin traction, commonly referred to

as “Buck’s traction” when used on the lower leg, a pulling force is applied to the limb in the form of adhesive tape, belts, or a foam boot. Weights are typically hung from a pulley system at the end of a patient’s bed. Limited force can be applied due to the risk of soft tissue irritation, especially in the elderly, usually not to exceed 8–10 lbs. Skeletal traction is more invasive but involves a more direct and greater pulling force on the bone through a surgically placed pin. This procedure is often done in the emergency department under local anesthetic or conscious sedation. Skeletal traction is the preferred temporizing treatment for femoral shaft fractures and unstable pelvic or acetabulum fractures until definitive fixation is performed. Skeletal traction is typically applied through the proximal tibia or distal femur under sterile conditions. Skeletal traction is more powerful than skin traction and allows pull of up to 20% of body weight [14, 22, 23].

19.6.5 Operative Treatment of Fractures

Although closed reduction and splinting techniques date back thousands of years, operative techniques have only come into the forefront over the past 100 years. With constant innovation and advancement of new orthopedic technologies and implants, injuries that previously resulted in significant limb threatening or functional impairment are now much less common. Achieving stable internal fixation now allows patients to mobilize earlier and allows for earlier range of motion of injured joints. There are many implant options for operative treatment of fractures, and choice of treatment depends on the fracture location and fracture type. Some of these include (1) external fixators, (2) internal fixation with screws and plates, or (3) intramedullary implants. To improve quality and consistency of surgical treatment of fractures in the 1950s, a group of orthopedic surgeons in Switzerland formed the AO (Arbeitsgemeinschaft für Osteosynthesefragen [Association for Osteosynthesis]) [24] . This meeting led to the development of the four AO principles of operative fracture management, which still hold true today:

1. Anatomic reduction of fracture
2. Stable internal fixation
3. Preservation of blood supply to the soft tissues and bone
4. Early and safe mobilization of the injured extremity [24]

Before discussing the various options for operative treatment of fractures, it is important to understand how fractures behave in different biologic and mechanical environments. Fracture healing can be divided into two types, primary and secondary, depending on the mechanical environment. *Primary*, or *direct*, bone healing occurs when the fracture reduction is anatomic, and the mechanical environment has *absolute stability* [25]. Absolute fracture stability can only be obtained with surgery. *Absolute stability* is achieved through implants that impart compressive forces, with minimal fracture gap and no motion across the fracture site under physiologic loads. Under absolute stability conditions, fractures heal by haversian cutting cones, and no callus formation occurs [25–27] .

Secondary, or *indirect*, bone healing occurs during conditions of *relative stability*. When the mechanical environment of the fracture has relative stability, very small interfragmentary motion can occur. Examples of relative stability environments include casts, splints, and several implants to be discussed below, including intramedullary nails and bridge plates. The small amount of motion at the fracture site is thought to stimulate callus formation seen on radiographs (Fig. 19.3). The stages of secondary bone healing include inflammation (1–7 days), soft callus (2–3 weeks), hard callus (3–13 weeks), and finally remodeling which can take months to years [25–27].

19.6.6 External Fixation

External fixation is a technique that uses large pins (4 mm or 5 mm) drilled through small skin incisions into bone with connecting rods and

Fig. 19.3 Retrograde intramedullary nail with callus formation at the fracture site

clamps to stabilize fractures. External fixation is widely used as a provisional treatment of many unstable fractures [28]. There are several indications which include (1) *damage control orthopedics*, (2) significant soft tissue injury, (3) contaminated open fractures, (4) unstable pelvic ring fractures, and (5) occasionally definitive management of certain fractures. *Damage control orthopedics* is a concept developed for the multi-traumatized patient that is too unstable for definitive fixation [28, 29]. It emphasizes early debridement of surgical wounds, with minimally invasive treatment (i.e., external fixation) of long bone fractures and joint dislocations until the patient is stable enough for definitive fixation [29].

19.6.7 Open Reduction and Internal Fixation

Open reduction follows the same principles as closed reduction, except that in open reduction, the bone is usually exposed through surgical dissection. Open reduction can further be classified as direct reduction and indirect reduction. *Direct reduction* is performed when fracture fragments are reduced under direct visualization. *Indirect reduction* is performed when fracture fragments are reduced without direct visualization. For example, an intraarticular fracture of a distal femur requires a direct reduction, because the joint surface needs to be in anatomic alignment to give the best functional outcome. However, an intertrochanteric hip fracture requires restoration of general length, alignment, and rotation and does not have to be "anatomic" for it to heal. This can typically be achieved with traction and indirect reduction techniques. The advantage of an indirect reduction is that it preserves the surrounding soft tissue and blood supply to fracture fragments. The disadvantage is that indirect reduction can often be more difficult since the surgeon is not directly visualizing the fragments and must rely on intraoperative fluoroscopy [30].

There are several implants that are used to provide internal fixation of fractures.

Kirschner wires (K-wires) are smooth, stainless steel pins that can be inserted into the bone using a power drill. They can be placed percutaneously or through an open incision. They are most often used to provide temporary, "provisional fixation" during open reduction procedures but can also be used for definitive fixation. For example, K-wires can be used to pin small bones, such as the phalanges in the hand or foot, or sometimes in certain pediatric fractures. Figure 19.4a shows a preoperative radiograph of a badly displaced supracondylar humerus fracture in a pediatric patient. Figure 19.4b is an intraoperative radiograph following closed reduction and percutaneous pinning with three K-wires. Pins are often removed after the bone has had time to heal.

Placement of *lag screws* is an internal fixation technique that provides rigid compression between fracture fragments. Lag screws are primarily utilized in two ways: (1) "lag by design" or (2) "lag by technique." Lag by design is achieved using a partially threaded screw that achieves purchase at the distal cortex of the bone, compressing the distal and proximal fragments together as the screw head is tightened. In lag by technique, the near and far cortex are drilled to different diameters. The far cortex drill hole is typically smaller, which allows the distal screw threads to purchase the distal cortex and compress the fragments.

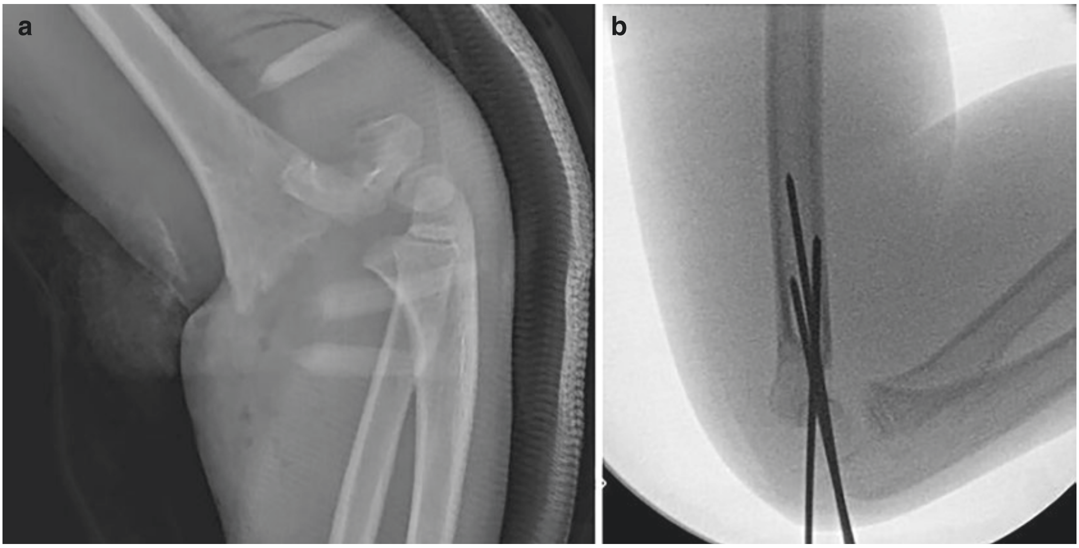

Fig. 19.4 (**a**) A displaced supracondylar humerus fracture in a pediatric patient. (**b**) intraoperative fluoroscopic image showing successful closed reduction and percutaneous pinning of supracondylar humerus fracture

With lag screws, the compressive force is concentrated over a small area (usually one screw) and can fail when torsional forces are applied. Therefore, lag screws are often combined with a plating technique called *neutralization*, or *protection plating*. With any plating technique a fracture is reduced and then fixed with a stainless steel or titanium plate and screws. Plates can be used in several different functions which include (1) neutralization (with a lag screw), (2) compression, (3) bridge, and (4) buttress.

A *neutralization*, or *protection plate*, technique is used in conjunction with a lag screw. This plating technique removes the loading forces on the fracture and transmits in through the plate, thus “protecting” the lag screw and allowing compression through the fracture site and primary bone healing to be achieved (Fig. 19.5).

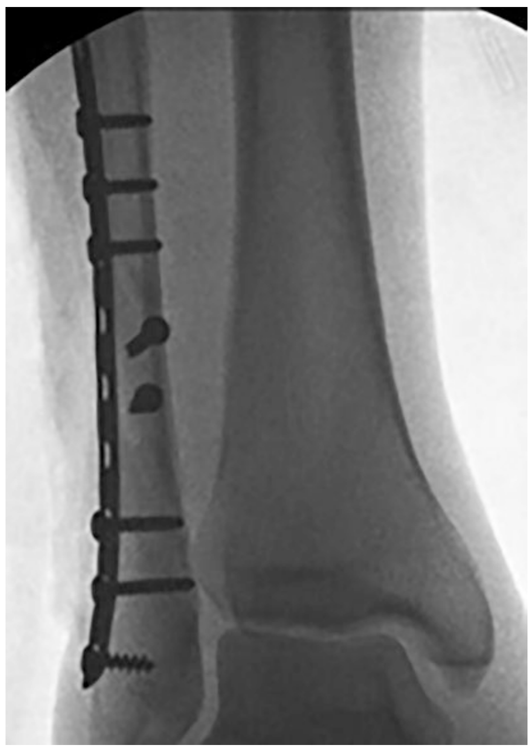

Fig. 19.5 Lag screw fixation of fibula fracture with neutralization, or protection plate, in place

A compression plating technique is used for simple fractures, typically a transverse or oblique pattern, that can be compressed. This plate has an oval hole design where screws can be placed eccentrically from the fracture. When

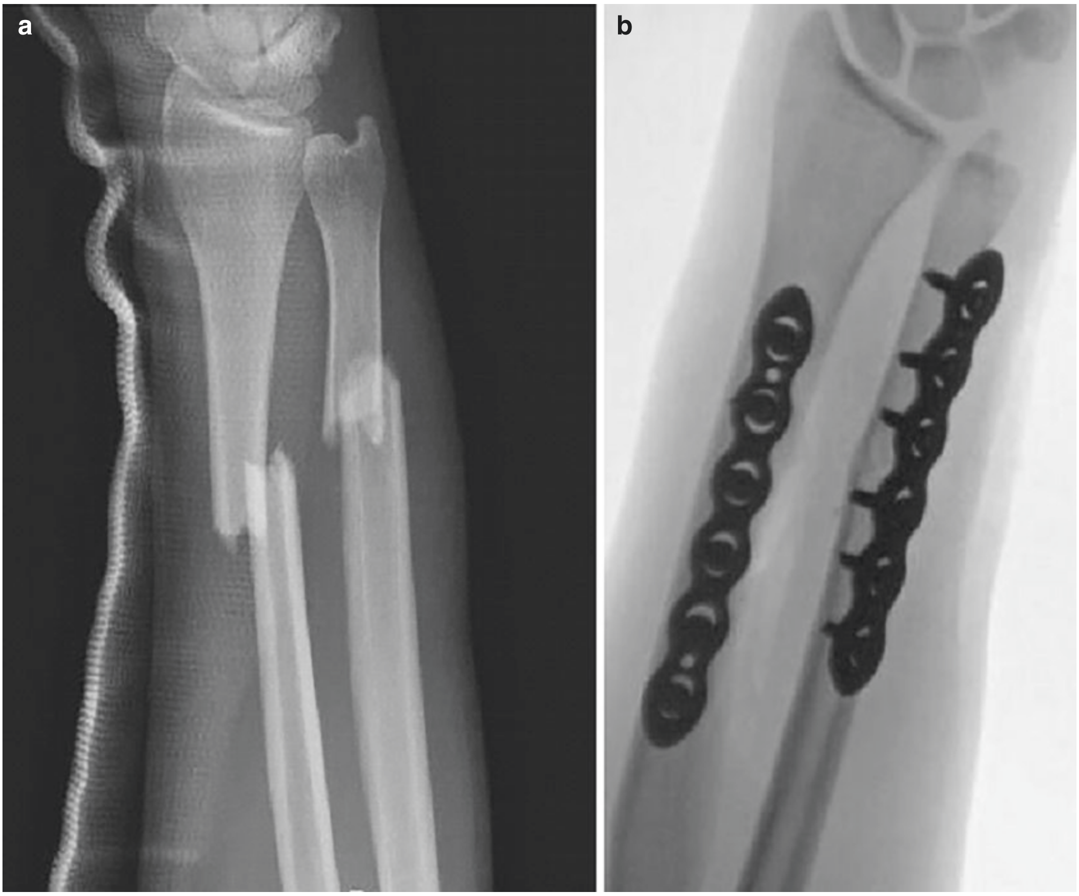

Fig. 19.6 (**a**) Transverse fractures of the radius and ulna. (**b**) Successful open reduction and internal fixation using compression plates

being inserted into the bone, the edge of the screw head glides down the edge of the screw hole and pushes the fracture site together. This can be repeated in another hole to gain more compression at the fracture site. When used properly, primary bone healing can be achieved (Fig. 19.6a, b).

A bridge plate technique is primarily used to span or "bridge" comminuted fractures. In these fractures, the bone is too fragmented to fix with lag screws or compression plates. In this technique, the plate is essentially used as an internal splint, allowing secondary bone healing to occur [31]. Oftentimes, this plating technique can be combined with minimally invasive or indirect reduction techniques to internally fix a fracture while not excessively disrupting the blood supply to the bone.

A buttress plating technique is used for shear-type fractures, where the plate provides support at a 90 degree. A buttress plate also applies compression to fracture fragments and can lead to absolute stability and primary bone healing (Fig. 19.7a, b).

19.7 Intramedullary Implants

Today, intramedullary nailing of most adult long bone fractures, especially the tibia and femur, is considered the standard of treatment. An intramedullary nail, usually made of titanium, is a load sharing device that is inserted into the medullary canal of the bone. After indirect fracture

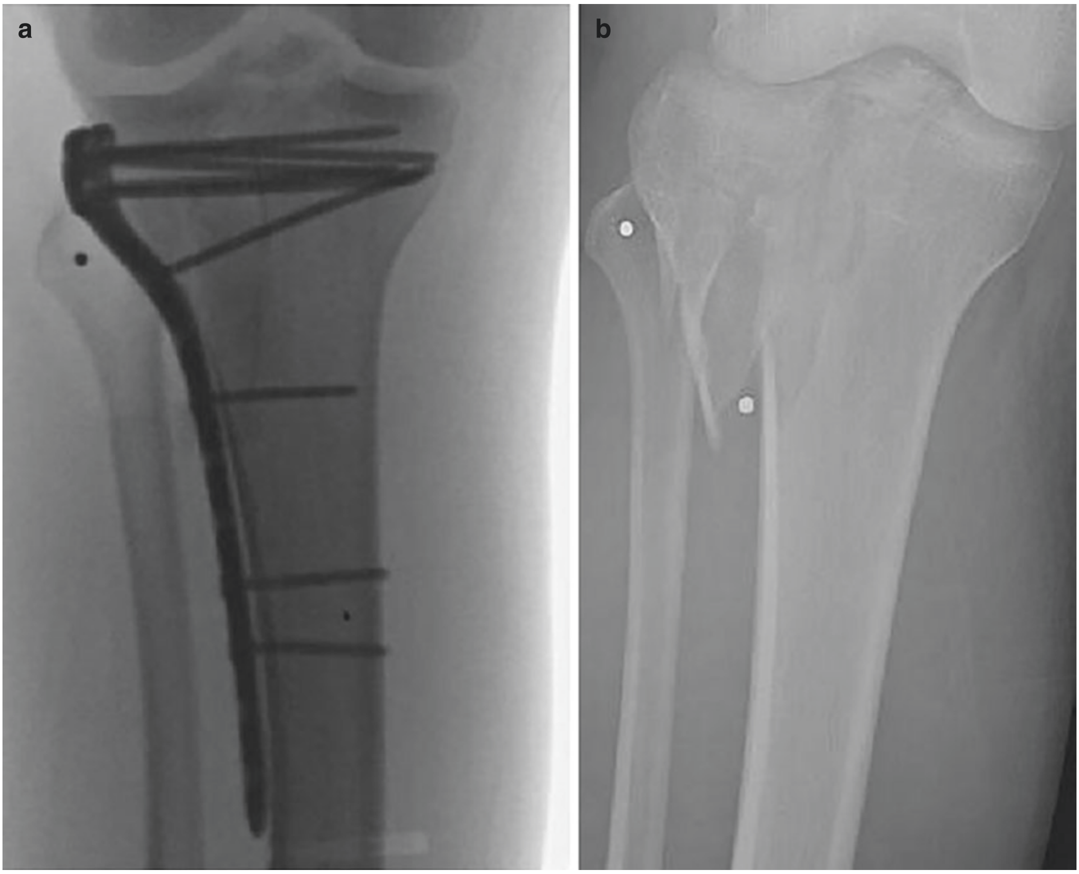

Fig. 19.7 (**a**) Lateral tibial plateau fracture. (**b**) Internal fixation of shear-type lateral tibial plateau fracture using buttress plating technique

reduction is achieved, the nail can be inserted in anterograde (from the greater trochanter) or retrograde fashion (through the knee) for a femoral shaft fracture. Intramedullary nails provide relative stability and lead to secondary bone healing. The benefit of an intramedullary nail is its minimally invasive insertion and allows for immediate weightbearing. The orientation of the intramedullary nail in the center of the bone allows for weight sharing between the bone and implant with ambulation. This is compared to a plate, which is applied eccentrically, on the cortex of the bone, resulting in a weightbearing device taking an asymmetrical load [32].

19.8 Pediatric Fractures

Fractures in children have certain unique features. Healing is more rapid and remodeling more extensive because of the higher levels of circulating growth hormone. Additionally, pediatric bones are constantly growing through endochondral ossification at the epiphyseal plate, or growth plate. The more growth remaining in a bone, the greater the potential for bone remodeling and therefore the greater amount of deformity that can be accepted following a given fracture. Other factors that affect the remodeling capacity of a fracture are its proximity to the epiphyseal plate and the direction of the deformity. Fractures near the epiphyseal plate, or with deformity in the plane of motion of the joint, have greater remodeling potential. Rotation is the deformity

least corrected by growth; therefore, rotational displacement is often corrected by closed reduction. Pediatric bones also have very thick periosteum, which can be used to aid in reduction maneuvers and exhibits greater osteogenic potential than that of adults.

Injuries to the epiphyseal plate are also unique to children. Since the epiphyseal plate is predominately made up of cartilage, it is more susceptible to injury. The *Salter-Harris classification* divides fractures into five types, based on the location of the fracture through or around the epiphyseal plate [33, 34]. If the fracture involves the epiphyseal plate, it may injure the proliferating cartilage cells, resulting in slowing or cessation of growth in all or part of the plate and a shortened or deformed limb [33, 34].

Because of the excellent healing and remodeling powers of children, open reduction, especially with internal fixation, is required much less often than in adults. Closed reduction and casting with or without temporary percutaneous pin fixation are more commonly used for definitive treatment.

19.9 Complications of Fracture Management

Operative and nonoperative treatment of fracture can be associated with several complications.

Complications of casts and splints include pressure ulcers if not well padded and loss of reduction, which can lead to a *malunion* [35]. *Malunion* refers to union with deformity (crooked bone), which usually results from inaccurate or "lost" reduction.

Union does not necessarily occur in a certain number of weeks or months following a fracture. Fracture healing depends on a great many variables. The location of the fracture and its morphology may play a big part in the timing of healing. The tibia has less surrounding muscle and therefore a decreased source of potential osteoblasts than the femur that is surrounded by muscle. An open fracture or a fracture with significant comminution may heal slower due to the lack of blood supply. Delayed union may be said to occur when, after a reasonable period of immobilization, bone union has not taken place [36].

Nonunion is a radiographic diagnosis characterized by failure of bone trabeculae to bridge the fracture site. Radiographically, the fracture line may increase in width and callus bridging the bone ends at the fracture line is not present. Whether a delayed union becomes a nonunion is temporal and depends on whether there is any progress toward improved bridging callus and bony union. Nonunions are characterized by a diminished blood supply to the fracture site, which may result from the injury itself or poor immobilization that allows the fracture fragments to shear off newly formed capillaries growing into the fracture callus [36].

Injury to regional nerves or vessels may be produced by the fracturing force, by sharp bone ends, by foreign object penetration, or by swelling.

Osteonecrosis of one of the fracture fragments occurs if that fragment is completely deprived of its blood supply by the fracture itself or its treatment. The three most common fractures that may undergo avascular necrosis secondary to a displaced fracture are the femoral head with femoral neck fractures [37], the talar body after a talar neck fracture [38], and the proximal pole of the scaphoid after a scaphoid waist fracture [39].

Infection may result from open fractures or the open treatment of fractures. As a rule, acute infections respond to antibiotic administration unless a purulent collection is present, whereas chronic lesions often require operative debridement of dead and avascular tissue in addition to antibiotic therapy. Long-term infections can lead to osteomyelitis of the bone and may require a more extensive debridement of the devascularized bone fragments. Orthopedic implants in place may harbor infection due to the presence of an avascular biofilm that bacteria can multiply in and is resistant to antibiotics (glycocalyx). In some cases, the implant must be removed after bony healing to completely eradicate an infection [40]. The most serious infections result from clostridial organisms, which may proliferate in ischemic tissue to produce a virulent myositis that results in loss of life or limb.

Tendon laceration by a displaced fracture fragment is infrequent, largely because of the

elasticity of the musculotendinous unit; however, tendon gliding may be impaired by fracture healing, and late rupture sometimes occurs in tendons moving over bony irregularities produced by the healing process [41].

Post-traumatic arthritis may follow fractures involving the articular surface of joints. This risk is reduced, although not eliminated, by anatomical reduction of such fractures [42]. With more severe injuries to the cartilage, there is an increase in the incidence of arthritis as hyaline cartilage does not regenerate.

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20 Rehabilitation of Musculoskeletal Injuries

Deborah L. Givens and Michael McMorris

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the principles of progression of rehabilitation of musculoskeletal injuries.
- *Objectives*: On completion of this unit, the learner should be able to describe, list, or identify the:

1. Components of the International Classification of Functioning, Disability and Health (ICF) model
2. Principles of progression of rehabilitation using protection, rest, ice, compression, elevation, and movement (P.R.I.C.E.M)
3. Interventions to restore mobility
4. Strength and endurance training principles that indicate a program is of sufficient intensity
5. Neuromuscular control principles
6. Outcomes that are related to restoring functional activity and participation

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20.1 Clinical Decision-Making for Restoring Activity and Participation

Musculoskeletal disorders are a significant cause of illness and missed work and affect morbidity, quality of life, and mortality [1, 2]. Chronic musculoskeletal pain (greater than 3 months) is a major health and socioeconomic burden. Approximately 25% of the world's population live with significant, chronic pain negatively impacting psychological health, quality of life, physical function, and work ability [3]. Musculoskeletal diseases make up the fourth leading contributor to disease burden in older adults. Between 1990 and 2010, this burden increased by 46%, resulting in significant challenges to maintaining physical activity [2].

20.1.1 International Classification of Functioning, Disability, and Health (ICF) Model

Physical activity has been associated with improved mental and physical health along with wellbeing [4]. Many body functions such as digestion, circulation, respiration, lymphatic circulation, bone health, and brain activity benefit from physical movement. Purported mechanisms for the benefits of physical activity include biochemical, physiological, and psychosocial factors. In contrast, individuals with musculoskeletal or other injuries that cause them to be physically inactive will have biochemical, physiological, and psychosocial factors that are impacted negatively. This impaired function can result in disability. According to the International Classification of Functioning, Disability and Health (ICF), disability is "an umbrella term for impairments, activity limitations and participation restrictions. It denotes the negative aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal factors)" [5]. The ICF model shifts focus *off the disease or condition* and *on to the negative impact on function*. The intention is not to undermine the importance of clinical diagnosis but rather to consider the interaction between multiple factors and their impact on activities. People are made to move; when they cannot physically function at their normal level, their health may be impacted physically, mentally, and/or socially [5].

Physical therapists and others use the ICF model to help organize information about health and health-related states, such as a musculoskeletal injury. The health condition "lateral ankle sprain (LAS)" is used to illustrate the model (Fig. 20.1). In the ICF model, *body functions and structures* refer to physiological and anatomical changes that occur with the condition or ankle injury (e.g., pain, swelling, loss of strength, and range of motion). *Activity* refers to the execution of tasks and actions (e.g., walking, running, hopping, or jumping). *Participation* refers to the ability to engage in life situations (e.g., work, recreation, community engagement, or social factors). Contextual factors of health are considered in the ICF model. These factors are divided into two components: environmental factors and personal factors. *Environmental factors* are external barriers or facilitators to the person's health in the context of the physical, social, and attitudinal circumstances in which the person exists (e.g., attitudes, services, support systems, or living environment) [5]. *Personal factors* are internal influences on function and disability (e.g., personal attitudes, habits, education, age, or sex).

Guided by the ICF model, the medical management of people with a musculoskeletal disorder should be informed by considerations beyond the label of the diagnosis or "health condition" perspective. The pain and disability from the initial injury impacts body functions and structures, activity levels, social participation, and the patient's psychoemotional wellbeing. The restoration of physical activity and functioning after musculoskeletal injury is important.

As an example, let's consider a specific musculoskeletal condition many people will experience at some point in their lives, lateral ankle sprain (LAS). LAS typically is the result of a forceful ankle plantar flexion and inversion leading to the damage of the lateral ligaments of the

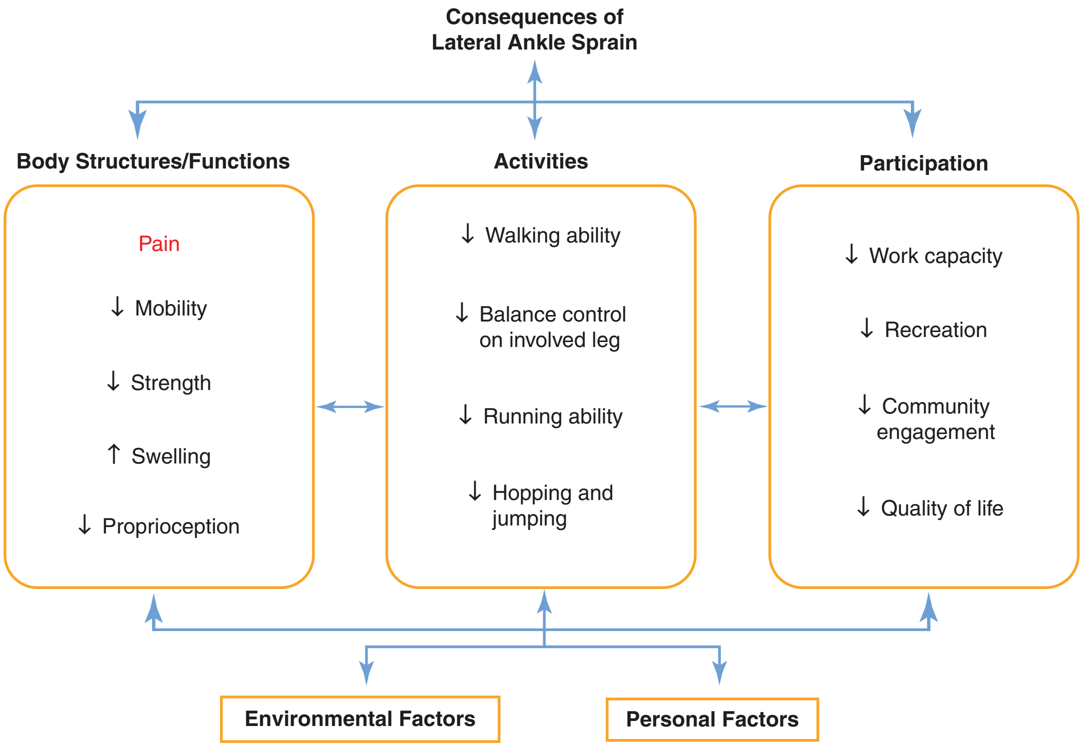

Fig. 20.1 Framework illustrating the application of the ICF model to a lateral ankle sprain

ankle. Most commonly injured is the anterior talofibular ligament followed by the calcaneofibular ligament and finally the posterior talofibular ligament. The consequences of LAS on activity and participation are broad as patients have difficulty bearing weight on the injured area, gait speed is reduced, and time off work is often required. Body function is impacted with a reduction in ankle range of motion and strength, increased pain, and altered joint proprioception, leading to impaired balance control during activities that require coordination and control of the involved leg. Recurrent ankle sprains are common – it is estimated that up to 75% of people sustaining LAS will have recurrence and develop chronic ankle instability [6]. Contextual factors that impact chronicity and injury risk include female gender, high body mass index, reduced ankle proprioception, playing athletics, playing athletics as a defender, greater height, and anatomic malalignment. LAS has a significant impact on patients physically, mentally, and socially [6, 7].

Rehabilitation of musculoskeletal injuries should be timely, holistic, patient centered, functional, and evidence based. In this chapter we will address the basic concepts of the rehabilitation of musculoskeletal injuries and assist you in setting expectations for patients you refer for examination and treatment.

20.1.2 Hypothesis-Oriented Algorithm for Clinicians

Rehabilitation of musculoskeletal injuries starts with the physical therapist making a sound assessment. Consistent with the ICF model, the therapist should take a complete medical history, perform a physical examination (body functions and structures), evaluate physical activity and participation, and consider the impact of environmental and personal factors. Rothstein et al. [8] present a sound framework utilizing science and evidence to guide clinicians. The hypothesis-oriented algorithm for clinicians (HOAC II)

guides practitioners to generate differential diagnostic hypotheses from *patient-identified problems (PIPs)*. Physical therapists should investigate PIPs through thoughtful questioning to determine the severity, irritability, nature, stage, stability, and functional impact of the problem. Before starting rehabilitation, it is important to confirm the etiology of the patient's complaint or that the causation is from a neuromusculoskeletal source. Upon completion of the patient interview, the physical therapist should generate a differential diagnostic hypothesis list, then use this to construct the physical examination. Utilizing clinical exam tools with stronger specificity (for ruling in a diagnosis) and stronger sensitivity (for ruling out a diagnosis), the physical therapist refines the differential diagnosis list and orders it by probability. At this point a treatment threshold is reached allowing a test intervention to be initiated for the leading diagnostic hypothesis.

20.2 Interventions Targeting Specific Components Impacting Activity and Participation

20.2.1 Principles of Progression

A common question from physical therapy students at the completion of the patient examination is: "How do we know where to start our treatment?" A typical progression in rehabilitation moves through the following phases – reduce pain → restore ROM → build strength and endurance → establish neuromuscular control → restore function. The patient examination should help determine the best course of treatment by meeting the patient where they are. A detailed interview and physical examination will reveal the patient's rehabilitative needs at that time.

20.2.2 Pain Reduction

20.2.2.1 Acute Pain and Inflammation

A musculoskeletal injury immediately triggers an inflammatory response which is the first step of many to healing. The goal of this response "is to eliminate the pathogenic initiator with limited collateral damage of the inflamed tissue, followed by a complex tissue repair to the pre-inflammatory phenotype" [9]. While working to return the body to a homeostatic state after injury, the signs of inflammation, calor (heat), rubor (redness), dolor (pain), and tumor (swelling) are typically present. Tissue damage and subsequent inflammation in a patient with musculoskeletal injury necessitate patient education in the protection, rest, ice, compression, and elevation of the area (or P.R.I.C.E.). The reported physiologic effects of ice include decreasing skin temperature, reducing blood flow and edema, slowing delivery of inflammatory mediators, reducing metabolic demand of hypoxic tissues, decreasing muscle spasm, and inducing a local anesthetic effect [10]. Admittedly, more evidence is needed to determine the effectiveness of protection, rest, ice, compression, and elevation therapy in acute injuries [11]; however, many feel it is a critical step in response to acute injury [12]. A small risk of complication does exist with cryotherapy. Common complications include allergic reaction, burn, intolerance, and frostbite. Additionally, caution should be used in patients with hypertension, mental impairment, or decreased sensation [10].

As the human body works to stop bleeding, remove debris, prevent infection, and prepare the wound environment for optimal healing, signs of this activity will be evident (pain, redness, swelling, heat, and loss of function). Depending on patient health, the nature of the injury, and numerous other variables, the inflammatory phase of healing may last for a few days to a month. During this period, rehabilitation should aim to enhance the healing process. In addition to the P.R.I.C.E. principles, common tools used during this phase include passive, active assisted and active range of motion, gentle joint mobilization, soft tissue mobilization, electric stimulation, and pulsed ultrasound.

20.2.2.2 Chronic Pain and Contextual Factors

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with

actual or potential tissue damage, or described in terms of such damage" [13]. A different path for rehabilitation may be selected if a patient has persistent pain, one lasting >12 weeks, and signs of ongoing tissue damage are absent. Historically, predictors of a poor outcome after musculoskeletal injury and subsequent chronic pain have included disability and a failure to return to work. The ICF's attention to contextual factors, environmental factors, and personal factors is useful for guiding the physical therapist's evaluation of chronic pain and its impact on functional activity and participation. Chronic musculoskeletal pain has a negative impact on mental and physical health producing subsequent decline in function [14].

The physical therapist will approach the patient with chronic musculoskeletal pain by considering how factors such as body structure, body function, social factors, and emotional factors are impacting activity and participation. Thus, biological (scar tissue, aberrant biomechanics, pathoanatomy), social (activities of daily living, work, family factors), or emotional (fear of movement, fear of returning to work, anxiety, depression) factors are examined and explored for their impact on the patient's ability to carry out activities of daily living or to participate in work or recreational activities. Consistent with the ICF model, a holistic approach to evaluating and treating patients with chronic pain is important. Historically treatment of chronic pain from musculoskeletal injury has been treated from a biomedical model where peripheral structural injury is the focus of interventions. This approach is inconsistent with current evidence supporting neurophysiologic changes in people with chronic musculoskeletal pain. Physical therapists have many tools to address neuroplastic changes including patient education to reduce fear and catastrophizing, cognitive-behavioral therapy, mindfulness, motor imagery, motor learning, peripheral sensory stimulation, and manual therapy [15]. Additionally, the rehabilitative team may include physicians, psychologists, physical therapists, occupational therapists, social workers, and other health professionals to guide the patient through the complexities of chronic pain [3].

20.2.3 Restore Mobility

Whether attending physical therapy for the first time or progressing through a rehabilitative process when a patient's primary issue is limited mobility, then the goal is to restore range of motion. Limiting factors to mobility after musculoskeletal injury include joint effusion, connective tissue shortening, joint mobility, patient fear/guarding, and pain. Because swelling is space occupying, it produces increased tension on tissues and restricts joint mobility. Care should be given to remove any causes of inflammation and treat with rest, ice, compression, and elevation. Additionally a compression garment or massage may be considered.

20.2.3.1 Range of Motion

Carefully controlled motion of the joint within the limits of pain-free range of motion (ROM) is often the focus of the acute, inflammatory phase after injury. Passive range of motion (PROM) is the movement of the joint that is produced entirely by a force external to the muscles affecting that joint (e.g., the therapist's hands, the patient's hands, a machine). PROM is often used in the earliest stages of injury (e.g., 2–7 days). Active ROM (AROM) is movement of the joint that is produced by muscles crossing that joint. AROM is not only beneficial for the muscle (elasticity and contractility), but there are benefits for bone and tissue stimulation (low loading) as well as circulation and prevention of thrombus formation [16]. Therefore, AROM should be initiated as soon as the motion is safe to be performed for the underlying or nearly bone or soft tissue.

20.2.3.2 Manual Therapy

Physical therapists utilize joint mobilization, also known as manipulation, to treat joint impairments that limit range of motion. The physical therapist uses knowledge of the joint's arthrokinematics ("motion at a joint occurs as the result of movement of one joint surface in relation to another"), osteokinematics ("refers to movement of the bones rather than the movement of the articular surfaces"), and the patient's clinical examination to determine the appropri-

ate manual therapy interventions. Assessment of accessory joint movements (or joint play) and whole joint motion helps determine if there are restrictions at the joint (capsule, articular cartilage, fibrocartilage, etc.) or overall movement (muscle, tendon, or connective tissue length) [16]. These assessments guide the selection of hands-on, passive skilled joint techniques (joint mobilizations) that the physical therapist applies based on an understanding of tissue healing rates and the potential for adhesions in the joint or ligaments as well as the patient's level of pain and muscle guarding. The mechanisms for manual therapy remain unclear. The proposed factors include mechanical stimulus, impact on peripheral nervous system, central nervous system response, endocrine response, and non-specific responses (i.e., placebo, patient expectation, kinesiophobia, etc.) [17].

20.2.3.3 Stretching

When functional mobility is limited due to soft tissues that have adaptively shortened, stretching exercises are indicated to elongate structures [16]. This tends to be a focus of the middle to later phases of rehabilitation. The physical therapist who is using joint mobilization to increase mobility will also introduce stretching exercises to help the patient maintain or advance the motion gained through their home exercise program. The goal is to prevent further adhesions and contractures by maintaining soft tissue extensibility. Common parameters for stretching exercises in musculoskeletal rehabilitation include that the stretch should be of low intensity (e.g., low load to just beyond the point of tissue resistance), sustained (e.g., 30 seconds), and of few repetitions (e.g., 1–3) [16, 18].

20.2.3.4 Case Application

Consider a 55-year-old female, recreational jogger with LAS 3 weeks ago. Numeric pain rating scale is 0–4/10 (best to worst), and pain gets worse when descending stairs, walking on uneven ground, squatting, and being on her feet more than 30 minutes at a time. Physical examination indicates limited ankle dorsiflexion; poor single-leg standing balance on the affected side; tenderness to palpation at the peroneal, anterior tibialis, gastrocnemius, and soleus muscles; as well as ankle weakness in all directions rated at 4-/5 with mild pain in all directions. Swelling, assessed with circumferential measurements, is minimal. This patient would be described as having a low pain severity and low pain irritability; therefore, her physical rehabilitation of LAS would start with restoring mobility. Physical therapy tools commonly used for this phase of rehabilitation include muscular stretching, joint mobilization, patient education for self-stretching, and proper positioning to avoid connective tissue shortening. Monitoring progress through rehabilitation of this musculoskeletal injury is based on the patient's improving health condition (LAS), healing body structures (ankle joint, lateral ligaments, leg muscles), increasing activity level (work, walking, going up-/downstairs), participation in life activities, and her confident ability to remain active without fear of re-injury.

20.2.4 Build Strength and Endurance

Physical therapists are trained to have a detailed eye for functional movements. When making initial introductions with the patient, the physical therapist will observe the patient sitting, getting up from a chair, and walking to the clinic room. Abnormal movement patterns are noted and these movements may be the patient's response to pain, a lack of range of motion, insufficient strength, or poor neuromuscular control. In the case of a patient with LAS, the ankle joint stiffness and loss of muscle strength limit the mobility and power available for propelling the body forward in space. This results in a slower gait and differences between the stride length of the involved leg compared to the uninvolved one. Hence, these preliminary observations provide insights into areas the physical therapist will examine in more detail for functional strength deficits and will reassess to determine whether the rehabilitation program is successful in ameliorating these deficits.

20.2.4.1 Strength Training Principles

Muscular weakness is assessed by manual muscle testing or hand-held dynamometry. Evidence supports muscles with normal nerve supply, which lack strength, respond well to strengthening throughout the lifespan. Numerous approaches to strengthening muscles exist and can be effective [16]. Many use a combination of isometric (stay in the same place), isokinetic (same motion/speed), and isotonic (same resistance) exercises. Incorporating both concentric (muscle shortening) and eccentric (muscle lengthening) contractions is important to address the function performed by muscles during daily activities. For example, when going upstairs, the gastrocsoleus muscle of the foot that pushes up from the step is concentrically active. When going downstairs the gastrocsoleus of the foot that remains on the step will be eccentrically active to lower the body.

In rehabilitation of musculoskeletal injuries with strengthening, the clinician should carefully select a patient-specific intervention plan for building strength. Early evidence recommended 3 sets of 10 repetitions with resistance of 75% of the 1 repetition maximum [19]. Current evidence recommendations vary from 40% to 60% of maximum effort to 60% to 80% of maximum effort with 2–3 sets of 8–12 repetitions [16]. The general principle of a higher load and lower repetition is necessary to build muscular strength.

20.2.4.2 Endurance Training Principles

Muscles need to be endurant in order for the individual to perform repetitive or sustained activities over time for daily function, work, or play. Endurance training involves a higher number of repetitions at a lower resistive load. An example would be a sub-maximal load for 5 sets of 30–50 repetitions [16]. Another approach to improving muscular endurance is to sustain isometric contraction for a prolonged period of time that is incrementally progressed over time.

20.2.4.3 Adherence and Education

Monitoring the contextual factors noted by the ICF model, attentiveness to facilitators, and barriers to exercise, as well as factors aggravating the patient's chief complaint guides selection of exercises. Knowing the *person* throughout rehabilitation is important. Is the patient someone who likes exercise? Do they avoid exercise at every turn? Has the patient tried rehabilitation numerous times and failed? These factors and more help with understanding the contextual factors that may impact adherence and should be considered when creating the rehabilitation program.

Patient education during rehabilitation is important and the alliance between the therapist and the patient is important for adherence to exercise. Patients often expect strengthening exercises to produce results at the same time as an intra-articular injection or oral pain medication. Physical therapists can modify patient expectations through education. Patients should be informed that it is normal to experience some discomfort while doing strengthening exercises. However, patients should learn to differentiate between a "good hurt" (exercise discomfort) and a "bad hurt" (overstressed tissues) to reduce fear of activity. With an appropriate dosing of strength and endurance exercises, patients can expect approximately 2–4 weeks of exercise to produce neuromuscular changes and up to 8 weeks for muscular changes [16].

20.2.5 Improve Neuromuscular Control

20.2.5.1 Motor Control

Neuromuscular control is a natural connection between the strength phase and return to function phase. Unlike strengthening where patients may be moving in a simple, singular plane of movement or a more complex movement with the intention of solely building muscular strength, neuromuscular control considers more variables. *Motor control* is "the ability to regulate or direct the mechanisms essential to movement" [20]. Through motor control the body must use sensory information to assess the position and motion of the body in space and execute the appropriate responses to control the body within

the environment and the task [16]. In our patient with LAS, this may take the form of adjusting her balance after stepping on a small pebble and avoiding a recurrent injury. Therefore, as pain and swelling subsides and strength improves, the physical therapist introduces varied balance-related exercises. Initial activities will include balancing on 1 foot, starting with a stable surface and progressing to a foam pad or wobble board [16]. Later activities will focus on the process of returning to running with the movements broken down into individual components as well as complex variations of running type movements.

20.2.5.2 Task Specificity and Practice Conditions

It is important that rehabilitation of musculoskeletal injuries is task specific (i.e., similar to or actually running/moving on varied surfaces or terrain), making the program more meaningful to the patient and more effective. Arranging the environment to replicate the actual setting will promote a more favorable outcome. In the effort to helping her reacquire the ability to dynamically control the hip-knee-ankle-foot, she needs a program promoting repeated performance (consistency), adaptability to changes in environment or conditions (variability), and musculoskeletal endurance (efficiency). To promote the acquisition of this motor skill, she needs practice. Evidence indicates that constant practice may produce less, long-term retention; therefore, variations of the task should be performed throughout a treatment session [20].

20.2.5.3 Feedback

Intrinsic and extrinsic feedback are important components to the neuromuscular control phase of rehabilitation [16, 20]. Our patient with LAS will naturally receive intrinsic feedback through her own sensory, visual, and auditory experience. Extrinsic feedback may come in many forms including verbal, visual, or physical cues. Verbal feedback may be prescriptive – offering information for her to improve the next repetition of the task – or descriptive, information on past performance. Visual feedback may be added with the use of a mirror which combines with intrinsic feedback or by the therapist modeling the behavior or movement. Finally, physical feedback in motor learning may be offered through manual guidance through movements [21].

20.2.5.4 Advanced Exercise

Guiding patients through the neuromuscular control phase of rehabilitation of musculoskeletal injuries is typically fun for the clinician and patient. By this time in the rehabilitation process, the patient's pain level is negligible, their strength has usually returned to ~75–80% of the premorbid level, and interventions integrate this available full range of motion and strength in new and challenging ways. In patients with upper or lower extremity injuries, they may improve neuromuscular control through plyometric exercise, balance activities, or multi-directional movements. *Plyometric exercise* in simple form is exercise with an eccentric pre-load followed by rapid concentric contraction such as jumping off a box to the floor and back up on a second box. Options for *balance activities* are numerous and may include standing on wobble boards or cushion pads while doing a second movement such as catching a ball. *Multi-directional movements* are considered to be complex actions with movement controlled through more than one plane and are movements that are required for skilled performance of many daily activities and sports. This is in contrast to simple, uniplanar movements that are often the basis of early exercise (e.g., leg lifts) or fundamental sports activities, such as passing a basketball. An example of an advanced, multi-directional movement exercise for return to sport is a single-leg squat followed by a jump and rotation in the air to land facing a new direction when passing the basketball.

In patients rehabilitating the upper extremity, neuromuscular control exercises will challenge the patient with resistance in multiple planes, varied positions, plyometrics, and response to perturbations. The more a patient's daily activity involves overhead motion, the greater the need for neuromuscular control exercises. Naturally, the overhead athlete rehabilitating an upper extremity musculoskeletal injury will progress through a complete neuromuscular control phase

in rehabilitation. The goal is to prepare the athlete's upper extremity for the extreme forces experienced in overhead athletics (throwing, tennis serve, volleyball spike, etc.).

20.2.6 Restore Activity and Participation

Applying the ICF model to rehabilitation of musculoskeletal injuries encourages physical therapists to take a multi-perspective, biopsychosocial approach to examination and treatment of patients. The model's emphasis on the whole person monitors interactions between the person's health condition, environmental factors, and personal factors and their impact on activity and participation. Restoration of functional activity and minimizing disability is the desired goal.

In the early phases of rehabilitation, when the focus is on healing, protection, and restoration of body structures/functions (reduce pain → restore ROM → build strength and endurance), evidence of progress will come from measures such as patient self-report of activity, pain ratings (numeric rating scales), range of motion, and manual muscle testing. As the patient with musculoskeletal injury works through the later phases (establish neuromuscular control → restore function), evidence of progress should focus on functional activity and participation. Assessment tools may include demonstration of activity, patient-reported outcome measures, or performance-based outcome measures. Some purported uses for information from standardized outcome measures include quality assurance, communicating with other healthcare providers, monitoring patient progress, and monitoring treatment effectiveness and research [22]. Patient-reported outcome measures are excellent ways to solicit the patient's perspective on satisfaction with care, their symptoms, functional status, and health-related quality of life. Patient involvement may increase self-efficacy and minimize observer bias [23]. Performance-based outcomes objectively measure patient activities (e.g., walking, lifting, jumping) as well as body function impairments (e.g., range of motion, strength, or balance) [24].

Our 55-year-old female runner has done significant work to restore motor control to her ankle and wants to get back to running trails soon. Seeing the patient perform the functional movement is an important step in understanding how to create a functional training progression. Possible interventions may include jogging in place, jogging on a rebounder, aerobic lateral step overs, jogging on a treadmill (flat and incline), and walk-jog training over ground. A focus on return to function in the rehabilitation process allows the patient to increase confidence in returning to physical activity without fear and lessened risk of re-injury.

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21 Management of Musculoskeletal Pain

Candy O. Ezimora and Ty L. Bullard

Contents

Goals and Objectives

- *Goals*: This chapter will provide a brief introduction to the physiology of acute pain, familiarize the learner with a multidisciplinary, multimodal approach to managing acute musculoskeletal pain, and delineate best practices for minimizing adverse outcomes related to prescription opioid therapy.
- *Objectives*: Upon completion of this chapter, the learner should be able to:
  1. Summarize the physiologic pain pathway.
  2. Understand different methods of evaluating pain.
  3. Describe the mechanisms of different pharmacologic modalities for treating acute pain, including: local anesthetics, NSAIDS, acetaminophen, neuromodulators, ketamine, glucocorticoids, alpha-2 agonists, and opioids.

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4. Describe several non-pharmacologic options for management of acute pain.
5. Understand the impact of widespread opioid use among the American public, and appreciate the role of the clinician in minimizing adverse outcomes related to prescription opioids.

21.1 Introduction

If there is perhaps one unifying quality of *Homo sapiens'* varied existence over time, it is that we have always suffered from pain. Comparatively intelligent, industrious, and impatient, we have sought relief from our ailments since the first prehistoric labor pains tortured new mothers and since the earliest of abscessed teeth nagged at our ancestors tens of thousands of years ago. For millennia, the treatment of acute pain consisted of a blend of trial and error, folklore remedy, and pseudoscience, just as authoritatively administered by monks, shamans, and snake oil salesmen as it was by early practitioners of medicine or pharmacology. Whether ultimately effective or not, and generally without regard to side effects, such treatments were almost uniformly directed at the scourges of the time: traumatic injury, infection, childbirth, and pain related to myriad and often unrecognized disease processes. Today, the most common settings for the treatment of musculoskeletal pain by physicians occur in the clinic or perioperative setting. While the initial presentation of acute pain to the practitioner is as old as medicine itself, acute post-surgical pain was rare until the industrial era of human civilization, if only for the simple reason that surgery itself was rare. Prior to the dawn of modern volatile-based general anesthetics, surgery was a brutal, dangerous, and horrific affair. As a result, emergency surgery was uncommon, and elective surgery was a relative non-entity. With the advent of general anesthetics in the mid-nineteenth century, the opportunities for surgeons to cure trauma and disease were vastly enlarged and enhanced. Even then, since burgeoning anesthetics were rare and as yet not widely adopted, routine elective surgery trailed their development by decades. Leading physicians and surgeons were slow to recognize both the transformative powers of anesthetics to relieve suffering and the potential of surgery to expand beyond its longstanding role as a last ditch effort.

Fast-forward to the present day: according to the latest national data available, roughly 25 million ambulatory surgeries and procedures were performed in the United States on an annual basis, and an almost equal number performed among inpatients [1]. Clearly, the advent of elective surgery in modern medicine has provided immense benefit to mankind and spawned a new and major sector of the health economy in almost every developed nation across the globe, lifting standards of living by virtue of the lifesaving surgical interventions themselves, as well as the economic boost measured in per capita GDP. Perhaps predictably, this explosion of surgical volume has also brought with it a floodtide of acute post-surgical pain. Against this backdrop, and with aggressive (or in some notable instances even false [2]) advertising to both patients and physicians, the prescription opioid crisis has engulfed the United States and many other wealthy countries. According to the CDC's 2018 Annual Surveillance Report of Drug-Related Risks and Outcomes, 2016 brought a record 63,632 drug overdose deaths, exceeding both motor vehicle and firearm-related deaths. Among those record-setting deaths, 66% were linked to opioids [3]. How can we as practitioners balance the benefit of treating acute pain with the risk of pervasive, destructive individual, and societal effects of opioid dependence and abuse? As increasing attention is paid to this question, our first responsibility as practitioners is to understand the fundamental nature of acute musculoskeletal pain and the pharmacology of commonly utilized drugs used to treat it. Importantly, we must also consider non-clinical contributors to pain and the therapeutic regimens that are currently available and indicated as we approach the patient presenting with acute pain.

21.2 Understanding Acute Pain

Pain may be defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage, a subjective experience that can be acute or chronic” [4]. Acute pain is generally understood to possess the following qualities: (1) an inciting event, (2) sudden onset, (3) time limited, and (4) the potential to develop into a pathologic condition. Pain is the culmination of a complex series of nociceptive pathways involving the cortex, brainstem, and spinal cord [5]. Conceptually, the pathway can be broken down into four components (see Fig. 21.1). With the inciting event, a noxious stimulus in the form of tissue damage is transduced into a nerve impulse, which is transmitted to the spinal cord by the peripheral nerves via the dorsal root ganglia. The spinal cord then modulates the signal as it carries it to the thalamus via the spinothalamic tract. Modulation occurs via neuronal connections within the periaqueductal gray, synapsing with descending inhibitory neurons that release

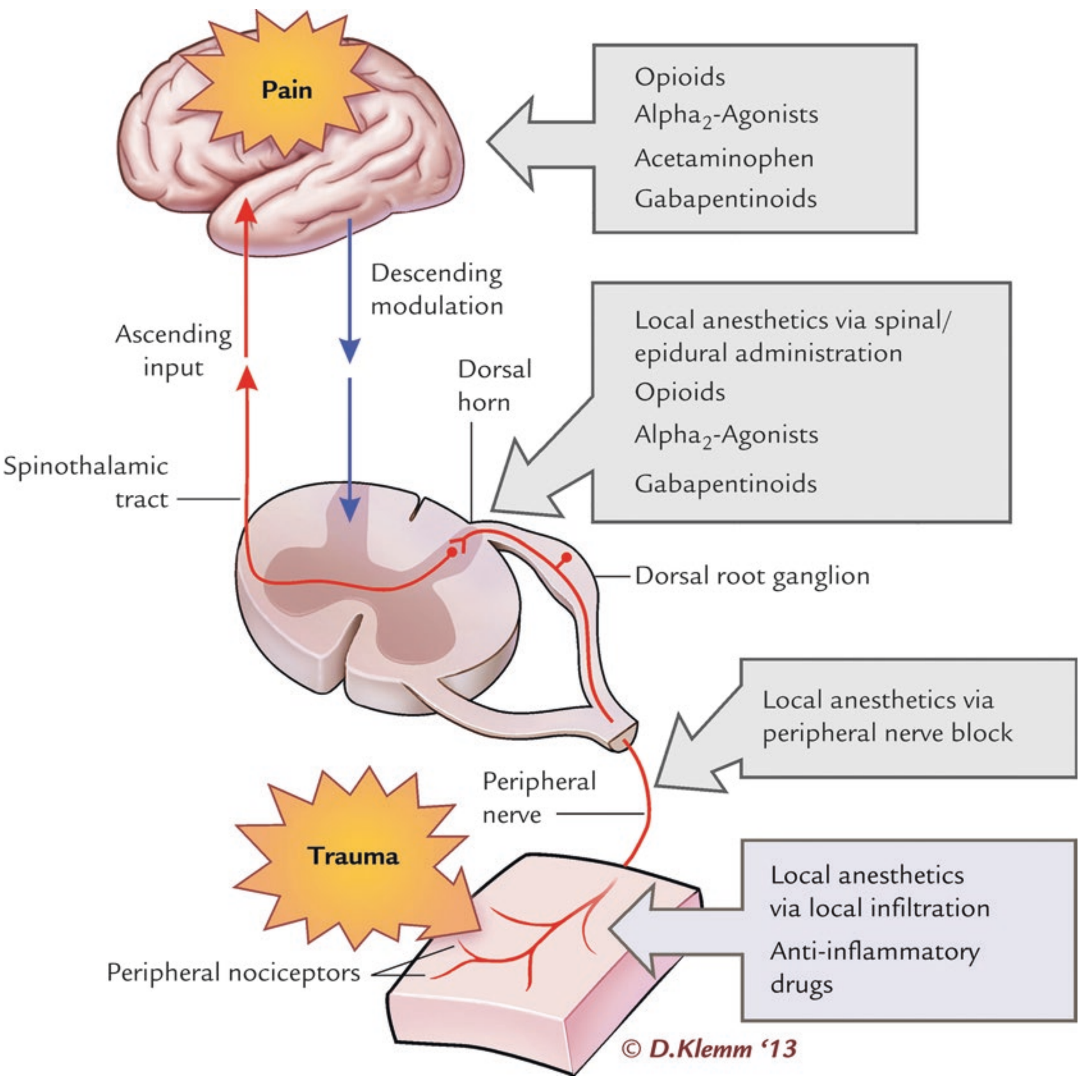

Fig. 21.1 A schematic of the pain pathway and the sites of action of different classes of analgesics. (Adapted with written permission from David Klemm, September 10, 2018)

endogenous opioids like enkephalin. Finally, the thalamus sends higher-order neurons to the cingulate gyrus and post-central gyrus in the cortex which facilitate perception of dull pain or sharp, localized pain, respectively [5, 6]. Bear in mind that this simplified model of the acute pain pathway is not comprehensive. Indeed there are many other neurotransmitters and molecules involved in the transmission, modulation, and perception of pain, but such detail is beyond the scope of this chapter (Fig. 21.1).

Recent trials have demonstrated better pain outcomes after improvement in symptoms of depression and anxiety [6, 7]. This is unsurprising when we consider that pain is a subjective response to nociception. As such, preoperative improvement in depression and anxiety (whether that involves optimizing patients' antidepressant regimen or addressing anxiety and pain expectations preoperatively) may lead to better postoperative pain control [8]. The role of psychosocial factors in the pathogenesis of pain, particularly chronic pain, is an area of ongoing investigation.

21.3 Measuring Pain

There exist numerous validated pain assessment tools to evaluate pain and track responses to treatment. These include numerical scales (the most common being the 0–10 scale), visual analogue scales, verbal rating scales, symbols, and others (see Table 21.1). No one assessment tool has been proven superior to alternatives. Therefore, it is important to utilize the tool best suited to the patient's developmental status, cognitive function, educational level, language, and culture, rather than the tool that may be closest at hand. The practitioner must understand the limitations of each pain assessment tool and acknowledge that pain tolerance and reporting are different for each patient. The qualification of pain is no less important than its quantification. The PQRST model provides a handy method of conceptualizing (and remembering) the qualitative components of pain (see Table 21.2). The final components of the overall pain assessment are to measure the response to intervention, to evaluate for any adverse effects of intervention, and to perform timely reassessments in an effort to achieve and maintain optimal patient comfort.

Table 21.1 Examples of commonly used pain assessment tools

Scale	Population	Description
Numerical rating scale	Adult and pediatric patients	Patients rate their pain on a scale of 0 (no pain) to 10 (worst pain imaginable)
Verbal rating scale	Adult and pediatric patients	Patients rate their pain intensity using one of five categories: no pain, mild pain, moderate pain, severe pain, unbearable pain
Visual analogue scale	Adult patients	Patients select a point on a 100 mm line that corresponds to their pain level (0 no pain, 100 severe pain)
FACES rating scale	Pediatric patients	Patients select one of six faces ranging in appearance from no pain (smiling face) to worst pain (grimace)

Table 21.2 PQRST pain assessment tool

PQRST component	Questions used for assessment
Provocation/ palliation	What makes it better? What makes it worse? Is it present at rest or with movement or both?
Quality	Is the pain dull and non-localized or sharp and localized? Is it neuropathic, visceral, somatic, or spasmodic?
Region/ radiation	Where does it hurt the most? Does the pain remain in one area or does or does it radiate to other areas?
Severity	How much does it hurt? Utilize one of the pain assessment tools here
Timing	When did the pain start? How long does it take for it to get severe?

21.4 Treating Pain

Multimodal analgesia involves the simultaneous use of multiple classes of analgesics that act independently and synergistically on variable and distinct receptors to block or modulate the pain impulse. Multimodal analgesic therapy

provides pain control that is superior to one medication alone [8–11]. In fact, multimodal analgesia has been shown to be more effective in treating postoperative pain when compared to opioid-based patient-controlled analgesia (PCA). The primary goal of modern multimodal analgesia is to control pain, to limit opioid consumption, and therefore to reduce the unintended adverse effects of opioid administration. The most commonly utilized multimodal agents include NSAIDs (Cox-1 or Cox-2 selective varieties), acetaminophen, gabapentinoids, NMDA receptor antagonists, alpha-2 agonists, local anesthetics, and, less commonly, steroids and magnesium. NSAIDs, acetaminophen, and gabapentinoids may be given preoperatively to preempt surgical pain and prevent peripheral sensitization associated with tissue damage [8, 12]. Regional and neuraxial (spinal, epidural, or paravertebral) anesthetic techniques are key components of a multimodal analgesia regimen where applicable [13]. While historically utilized most commonly in the orthopedic setting, regional and neuraxial techniques are increasingly utilized across many surgical subspecialties as dermatomal anatomic relationships are better understood, and as minimally invasive ultrasound-guided capabilities and delivery devices continue to improve.

21.4.1 Local Anesthetics

Local anesthetics provide analgesia by blocking voltage-gated sodium channels at the level of tissue injury, peripheral nerve, or the spinal cord, thereby inhibiting nerve conduction and transmission of the pain signal [10]. Local anesthetics are classified broadly based upon their structure and mechanism of elimination. Structurally, local anesthetics may be either ester-based or amide-based. Ester local anesthetics, containing a carbon-oxygen-carbon ester linkage, are eliminated by plasma esterases. Amide-based local anesthetics are far more commonly utilized in the clinic and perioperative setting and are eliminated after modification in the liver. True allergic reactions to local anesthetics are uncommon, but occur at higher frequency among the ester local anesthetics. The astute clinician will learn to differentiate true allergic reactions to local anesthetics from commonly reported non-allergic adverse reactions to additives, such as epinephrine, that are commonly utilized in the outpatient or dental settings. Local anesthetics vary in their toxicity profiles, with toxicity generally increasing with duration of action. Most life-threatening reactions occur after inadvertent intravascular administration, which may occur during intended peripheral nerve blockade, subcutaneous injection, or any other planned route of administration. Local anesthetic systemic toxicity (LAST) presents initially with tinnitus and/or perioral numbness and progresses to neurological symptoms such as lightheadedness, paresthesias, visual and auditory disturbances, agitation, confusion, seizures, and coma. Severe toxicity may result in cardiac signs or symptoms including an increased PR interval on ECG and hemodynamic instability and may culminate with cardiac arrest manifested by ventricular fibrillation [10]. Cardiac arrest secondary to LAST in the setting of long-acting amide local anesthetics such as bupivacaine or ropivacaine is notoriously difficult to treat. This is thought to be secondary to the intense binding capabilities of these drugs to cardiac conduction pathways [10]. Treatment consists of supportive therapy guided by ACLS, as well as immediate administration of intravenous intralipid, which can be lifesaving [14].

Local anesthetics may be delivered by various modalities, but the most commonly utilized methods within the context of orthopedic surgery are by the surgeon via (1) local skin or incisional infiltration or (2) periarticular infiltration, and by the anesthesiologist via (3) perineural infiltration via peripheral nerve blocks or (4) neuraxially via spinal or epidural approaches. Notably, intra-articular infiltration with amide local anesthetics has been linked to chondrolysis, and has since fallen somewhat out of favor [10]. The most commonly utilized local anesthetics with these techniques include lidocaine, bupivacaine, and ropivacaine. Each varies in their onset, elimination half-life, and duration of action (Table 21.3).

Table 21.3 Local anesthetic onset and duration of analgesia [15]

			Duration of analgesia	
Local anesthetic	Ester/amide	Onset (minutes)	Peripheral nerve block (hours)	Spinal (minutes)
2-Chloroprocaine	Ester	10–15	2–3	<60
Mepivacaine	Amide	10–20	3–8	–
Lidocaine	Amide	10–20	3–8	60–90
Ropivacaine	Amide	15–30	5–24	–
Bupivacaine	Amide	15–30	6–30	90–120

Duration of action is additionally dependent upon the route of delivery, dosage, and the use additives.

A major drawback of local anesthetics is their restriction to administration in the clinic or hospital setting, resulting in a finite and relatively short duration of action. Prolongation of sensory blockade can be achieved with additives including clonidine, dexamethasone, and epinephrine [8]. Continuous infusion of local anesthetics through indwelling peripheral nerve catheters has also been demonstrated to reliably prolong local anesthetic blockade, reduce pain scores, and limit opioid consumption [12]. Additional benefits of continuous infusions may include decreased nausea and vomiting, increased patient satisfaction, and decreased rates of hospitalization or readmission for pain [6]. Drawbacks of continuous infusion include the requirement for technical proficiency to place the catheters, expense, patient inexperience, pump failure, lack of programmability, and the sometimes unpredictable nature of drug delivery associated with ambulatory infusion devices [10]. While rare, permanent nerve injury, tissue necrosis, cellulitis and infection, and retained catheters have also been reported. Persistent weakness, numbness, or paresthesias after peripheral nerve blockade are worrisome to patient and clinician alike, though almost all instances resolve completely over a period ranging from days to months.

The addition of sodium bicarbonate to local anesthetics as a buffering agent is reported by patients to result in less pain on injection and a faster onset of action when used for skin infiltration. Different local anesthetics may be used in conjunction in order to achieve a combination of quick onset and long duration. Despite widespread practice habits to the contrary, local anesthetics should not be combined in the same syringe, as this leads to difficulty in calculation of safe maximum dosing of individual agents. When using multiple agents, it is critical to remember that maximum doses are additive and must be reduced accordingly.

Liposomal bupivacaine utilizes a unique mechanism for the sustained release of long-acting local anesthetic without the need for indwelling catheters and continuous infusions. The drug is encapsulated in liposomal vesicles that slowly release the active molecule over roughly 72 hours. Liposomal bupivacaine is used extensively in abdominal surgery and thoracic procedures by incisional infiltration. Periarticular infiltration in total knee arthroplasty has also been well described with encouraging results. More recently, liposomal bupivacaine has been FDA approved for use with interscalene peripheral nerve blocks for shoulder arthroplasty [16]. Liposomal bupivacaine has been shown to be associated with less pain, less opioid consumption, and shorter hospital stay when compared with traditional peripheral nerve blocks [10, 16]. The most common side effects associated with liposomal bupivacaine are nausea and vomiting. Although no studies have demonstrated neurologic or cardiac toxicities after administration of liposomal bupivacaine, it is important to understand that all local anesthetics have the potential to cause life-threatening systemic toxicity, and care should be taken when administering them in any form [10].

21.4.2 NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase to relieve inflammation and block nociceptive stimuli. They are often used as first-line treatment for mild-to-moderate

Table 21.4 Selectivity of commonly used NSAIDs

COX-1 selective	Nonselective	COX-2 selective
Ketorolac	Ibuprofen	Diclofenac
Ketoprofen	Fenoprofen	Celecoxib
Indomethacin	Sodium salicylate	Meloxicam
Aspirin		Etodolac
Naproxen		

pain and can decrease concomitant opioid consumption by up to 30% [6, 8]. NSAIDs are available in oral, intravenous (IV), and intramuscular (IM) formulations. Administration of NSAIDs in the acute pain or perioperative setting is often limited by their significant side-effect profile. NSAIDs may be predominantly COX-1 selective, COX-2 selective, or nonselective (see Table 21.4). Increased risk of bleeding as a result of platelet dysfunction is the major side effect of COX-1 selectivity. Nonselective NSAIDs such as ibuprofen are also associated with an increased risk of gastrointestinal bleeding and ulceration, cardiovascular events, and renal dysfunction [6, 8, 10, 12]. COX-2 selective NSAIDs, such as celecoxib and diclofenac, were developed to mitigate the bleeding risk associated with traditional NSAIDs, although they demonstrate an increased risk of cardiovascular events compared to more COX-1 selective agents. Historically, NSAIDs have played only a minor role in pain management for orthopedic surgery patients in the immediate perioperative period due to their correlation with bone nonunion in animal studies, though this has not been demonstrated reliably in humans [10, 12]. In recent years, however, as practitioners seek viable alternatives to oral opioid therapy, NSAIDs are increasingly important adjuncts in the outpatient and perioperative setting, especially when considering the relatively low side-effect profile of the COX-2 selective family of agents [9].

21.4.3 Acetaminophen

Acetaminophen is an antipyretic analgesic without significant anti-inflammatory effects. Its analgesic effects are thought to be derived from serotonergic activation and central prostaglandin inhibition, though the mechanism of action is yet to be clearly elucidated [6]. Acetaminophen is an integral part of any multimodal analgesic regimen and has additive, though not necessarily synergistic, effects with NSAIDs. When used in conjunction with opioids, acetaminophen may significantly reduce the opioid requirement, particularly when administered on a scheduled basis rather than as needed [1, 6, 8]. Doses should not exceed 4 g per day in adults or 90 mg/kg/day in children under the age of 12, as excessive doses are associated with liver dysfunction and/or failure [10]. Intravenous acetaminophen is particularly effective in treating moderate to severe pain in orthopedic patients who cannot tolerate oral medications [6]. Preoperative oral acetaminophen has been shown to have similar analgesic potential and opioid-sparing effects as the intravenous formulation and at the time of writing is far more cost-effective [6]. As such, the routine administration of IV acetaminophen should be limited to those scenarios in which the oral route is either unavailable or impractical.

21.4.4 Neuromodulators

Neuromodulating drugs such as gabapentin and pregabalin provide analgesia by inhibiting the **α**-2-**δ** subunit of the calcium-gated channels on presynaptic axons [6]. Although not FDA approved for treatment of acute pain, they have become an important component of multimodal analgesia. They can be given preoperatively and may be beneficial when provided on a scheduled basis postoperatively. Both drugs are available only in the oral form, potentially limiting their use in the immediate postoperative period. Both gabapentin and pregabalin are associated with dizziness and sedation, especially in the elderly [9]. Dose reductions are required in patients with renal dysfunction. Recent evidence has suggested that gabapentin at high doses may be associated with respiratory depression when used for treatment in the elderly and patients with chronic lung disease or renal disease [11]. Respiratory depression was particularly significant when moderate-to high-dose gabapentin was coadministered with opioids. In fact, coadministration was linked to a

substantial increase in opioid-related deaths [11]. Despite its lower incidence of sedation, similar correlations have been recently demonstrated with pregabalin when coadministered with opioids [17]. These findings warrant caution for the use of gabapentin and pregabalin in the perioperative period, especially where outpatient opioid therapy remains a mainstay of postoperative analgesia.

21.4.5 Ketamine

The NMDA receptor has been implicated in the development of chronic and neuropathic pain through its role in central sensitization and spinal cord hyperexcitability [6]. Therefore, blocking or modulating the activity of the NMDA receptor is an effective strategy for treating acute postoperative pain and for potentially preventing the development of chronic pain. Although multiple agents including magnesium, dexamethasone, and methadone all possess NMDA receptor-antagonism properties, ketamine has emerged as the preferred NMDA receptor antagonist used for the treatment of acute pain in patients who are opioid tolerant. Ketamine has been shown to improve postoperative pain when used alone or in conjunction with opioids [6]. It is opioid-sparing as well as effective against postoperative nausea and vomiting [6]. The use of ketamine is limited to the inpatient or directly observable clinical setting, as it is a scheduled drug most commonly administered in the IV form. It is commonly used in the emergency department environment to provide brief, potent analgesia with relative hemodynamic stability and preservation of respiratory function. In this context, it may be an excellent choice for the closed reduction of fractures. Caution must be exercised when administering ketamine to hemodynamically compromised patients, however, as its relative stability is dependent upon the stimulated release of endogenous catecholamines, which may be depleted in the acutely volume compromised patient. Intraoperatively, ketamine is utilized as a component of multimodal analgesic regimens and is typically administered as an IV bolus dose prior to incision, with or without continuation as an infusion throughout the procedure. It has also been successfully used in the ICU as a tool to wean patients from opioid infusions. While much less common, ketamine may also be administered via other routes including, in order of descending bioavailability, IM, subcutaneous, intranasal, rectal, and oral. Adverse effects are dose dependent and may include excessive sedation, dissociation, diplopia, nystagmus, dizziness, hallucinations, and nightmares [10].

21.4.6 Glucocorticoids and α-2 Agonists

Glucocorticoids are endogenously released from the adrenal cortex during periods of stress. Although they are not the first-line agents for acute pain, synthetic exogenous glucocorticoids can be administered as adjuncts to traditional analgesics, especially in patients with suppressed adrenal function [12]. Glucocorticoids act by reducing inflammation, thereby modulating the cascading pathophysiology of pain. Some, like dexamethasone, also act as NMDA receptor antagonists [6]. Glucocorticoids have also been shown to reliably reduce postoperative nausea and vomiting [12]. Adverse effects of glucocorticoids include suppression of endogenous steroid production, hyperglycemia in susceptible patients, poor wound healing, and increased susceptibility to infection [12].

Clonidine and dexmedetomidine are central α-2 agonists that are effective for the treatment of pain when used as components of a multimodal regimen, as well as additives to local anesthetics for neuraxial and peripheral nerve blocks [6, 8, 10]. Clonidine has been shown to prolong the duration of a single-shot peripheral nerve block by up to 2 hours [8]. More recently, dexmedetomidine, which has eight times more specificity for the α-2 receptor, has been shown to significantly speed onset and increase depth of both motor and sensory peripheral nerve blockades, as well as to prolong the duration of analgesia when

combined with local anesthetics [18, 19]. Both clonidine and dexmedetomidine are associated with increased risk of transient bradycardia, hypotension, and sedation [6, 8, 18, 19].

21.4.7 Opioids

Despite the current evolution of perioperative prescribing habits, opioids persist as a mainstay of acute pain management, particularly in the postoperative period [10, 12]. Although opioids of differing classes vary in their speed of onset, duration of action, and path of elimination, they are all similar in their activation of the centrally located **μ**-opioid receptor in order to provide analgesia. Opioids are available in many formulations and can be administered by almost any route, including oral, sublingual, intravenous, intramuscular, rectal, and neuraxial. Intravenous and oral routes remain the most popular options for the management of acute pain. Opioids administered via patient-controlled analgesia (PCA), where patients have some control of their analgesic regimen, are associated with improved pain management and increased patient satisfaction when compared with healthcare provider-administered IV opioids. However, PCAs do not mitigate the risk of opioid-related adverse effects, including respiratory and central nervous system depression, nausea, vomiting, pruritus, and impaired gastrointestinal motility [8, 10, 12]. PCA, specifically bolus dosing of morphine or hydromorphone *without* a basal infusion, is the preferred modality when opioids must be administered via the IV route. However, most evidence suggests that the IV route is not superior to oral with regard to analgesic effect [8]. Intravenous opioids provide a clear advantage in the immediate postoperative period when more rapid onset of pain relief is desired and where the oral route may be unavailable.

Opioid analgesia may also be administered via the neuraxial route, either with or without the concurrent administration of local anesthetics. While attractive options for any procedure below the waist, spinal or epidural routes are particularly useful in orthopedic patients presenting for total knee or total hip replacements, as these procedures are common among patients presenting with multiple medical comorbidities that may make general anesthesia a less desirable option [8, 12]. Epidural and spinal opioid analgesia decreases the risk of postoperative mortality, venous thromboembolism, respiratory depression, prolonged ileus, and postoperative pulmonary complications when compared to systemically delivered opioid therapy [8]. As with all opioid routes, neuraxial administration is not free of adverse effects. Patients should be monitored for respiratory depression, hypotension, and neurologic symptoms of spinal cord compression resulting from infection or hematoma. Such symptoms may be difficult to elicit after lower extremity surgery.

Tramadol, a morphine derivative, is of growing interest for pain management in orthopedic patients due to its **μ**-opioid agonist activity associated with fewer undesirable side effects [6, 9, 12]. Importantly among these, tramadol is thought to have less potential for abuse than traditional opioids. Tramadol inhibits reuptake of serotonin and norepinephrine so it must be used cautiously in patients taking other SSRIs and SNRIs so as not to precipitate serotonin syndrome.

Transdermal and sublingual opioid delivery devices, often utilizing fentanyl, are FDA approved only for use in chronic pain and addiction and should never be used to treat acute pain. One exception may be when utilized as a component of acute pain treatment in the setting of a pre-existing chronic pain indication. Use of extended release formulations of potent oral synthetic opioids in the acute pain setting may result in catastrophic respiratory depression and death, as these drugs are not titratable once administered. This rationale applies to any extended-release formulations, including both MS-Contin and Oxycontin, despite the all too common and widespread use of these agents to treat acute postoperative pain.

21.4.8 Non-pharmacologic Modalities

The management of acute musculoskeletal pain should not consist in a purely pharmacologic approach. Physical modalities such as acupuncture, exercise, massage, and transcutaneous electrical nerve stimulation (TENS; portable devices that deliver low-voltage electrical currents through the skin) may play a role as adjuncts in patients with both acute and chronic pain [6, 8, 9, 12, 20]. With the exception of TENS, the evidence regarding the effectiveness of these modalities in patients with acute pain varies significantly and more research needs to be done [11]. Nevertheless, they may provide some benefit, are widely considered safe, and can therefore be recommended to the appropriate patients based upon clinical judgment.

21.4.9 Outpatient Pain Management

Pain management for most orthopedic surgery patients often precedes surgery and continues well after they have been discharged from the hospital. The outpatient treatment plan must provide appropriate pain coverage and allow patients to slowly transition back to baseline function, if possible. Most of the aforementioned analgesics that are available in oral formulations may be prescribed in the outpatient setting, but acetaminophen and NSAIDs remain the most popular and effective non-opioid agents. It is imperative to educate patients regarding the safe use of any and all analgesics while monitoring for possible side effects. It is also important to provide patients with basic protocols for tapering analgesics as they progress further from their injuries and surgery. Unfortunately, there is no universally accepted schedule or protocol, so tapering must be individualized. Additionally, it is generally recommended that patients not on long-term opioids prior to their injury or surgery receive no more than 1–2 weeks' supply of opioids [8]. As previously mentioned, continuous infusion of local anesthetic via various outpatient delivery devices may be an option for some patients postoperatively, but also requires the relevant personnel and infrastructure for placement, as well as extensive patient education regarding management of the device. Additionally, patients must be prepared for the associated sensory and motor deficits that accompany effective local anesthetic analgesia. Finally, pain management should be part of the greater outpatient treatment plan that includes physical rehabilitation, psychosocial assessments, follow-up visits at appropriate intervals, and effective transition back to the care of the primary care provider [12].

21.5 Acute Pain and the American Opioid Crisis

In October of 2017, the President of the United States declared the opioid crisis a national emergency, at last unlocking federal funds to be targeted at opioid-related deaths and addiction. While deaths from prescription opioids have begun to plateau around 20,000 per year, those from powerful synthetic opioids like fentanyl – the most common opioid used intraoperatively – are increasing dramatically and are expected to rise further in the decades ahead [21]. One might reasonably ask how we arrived at this point, whereby the fruits of modern medicine have dealt us deadly and unintended consequences. The shaping of thought around the prescription of powerful opioid analgesics has been in motion for many years. In 1980, in a letter to the editor of the *New England Journal of Medicine*, authors Porter and Jick reported that in a survey of their hospitalized patients, the rate of addiction after prescription opioid use was extremely low, at 4/11,000 [22]. That estimate has been shown to be a gross underestimate, with the figure in more recent and robust studies in some cases exceeding 10% [23, 24]. Cited many times since its original publication, and put to use alongside aggressive opioid marketing tactics that have in some instances shown to be blatantly fraudulent [2], the Porter and Jick letter contributed significantly to the idea among prescribers that outpatient opioid use was largely free of serious risk. While the national crisis is multifocal in its ori-

gins, physician prescribers must shoulder some of the responsibility. In many instances, the first opioid exposure reported by patients suffering from addiction came from a legitimate prescription, either for themselves or for someone else. Unquestionably, physicians of the twenty-first century must have a clear understanding of the extraordinary burden represented by opioid dependence and addiction, both in terms of the cost to governments and society at large, as well as the devastating toll in human lives. The utilization of non-opioid analgesics in combination with non-pharmacologic interventions should always occupy first-line treatment for the vast majority of acute pain presentations. While opioids will continue to play an important role in the treatment of acute pain, particularly in the perioperative setting, their use should be weighed against the potential life-threatening risks that they present. Prescribers should continuously re-evaluate their clinical necessity at every opportunity and seek alternatives wherever possible.

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Part V

Clinical Conditions of the Musculoskeletal System

22 Common Pediatric Conditions and Evaluation of the Limping Child

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Contents

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Goals and Objectives

Goal: To introduce the reader to principles of evaluating a limp in a child along with common musculoskeletal conditions in pediatric patients.

Objectives: Upon completion of this chapter, the learner should be able to describe, list, or identify:

1. The development and progression of gait in children
2. Components of the physical exam used to evaluate a limp in a child
3. Differential diagnosis for a painful limp in a child
4. Differential diagnosis for a painless limp in a child

22.1 Introduction

Limping is a common reason for parents to bring a child to the pediatrician, emergency department, or orthopedist. The differential for a limping child is long including trauma, infection, or malignancy, which requires urgent treatment (Table 22.1). Alternatively, a limp may be secondary to a weakness, mechanical abnormality, or a neuromuscular condition. A systematic approach to the evaluation and diagnosis of a limping child is vital in order to arrive at the correct diagnosis and avoid a delay in treatment.

22.2 Normal Gait

The normal gait cycle is age dependent. As children begin to walk between 12 and 18 months of age, they have a wide-based stance with short stride length and rapid cadence [1–4]. By about 3 years of age, a child develops improved balance and abductor strength to allow them to spend more time in single-leg stance and thus stance narrows and cadence slows [1, 3, 4]. Most children display a mature gait pattern by 7 years of age [1–4].

In the mature gait cycle, about 60% of the time is spent in stance phase, while about 40% of the time is spent in swing phase [1, 3, 4]. Stance phase can be broken down into the initial contact, the loading response, mid-stance, terminal stance, and pre-swing. During initial contact, the ankle is dorsiflexed while the knee and hip are both slightly flexed [3, 5, 6]. As the center of mass is brought over the foot in mid-stance, the hip and knee extend. During single-leg stance, the abductors stabilize the pelvis, keeping it level while the opposite limb is advanced forward during its swing phase [4, 7, 8].

Table 22.1 Differential diagnosis of a limping child

Trauma	Toddler's fracture
Infection and inflammatory conditions	Septic arthritis Osteomyelitis Discitis Transient synovitis Juvenile idiopathic arthritis (JIA)
Anatomic disorders	Developmental dysplasia of the hip (DDH) Legg-Calve-Perthes Coxa vara Slipped capital femoral epiphysis (SCFE) Limb length discrepancy Osteochondritis dissecans Discoid meniscus Tarsal coalition Overuse syndromes
Neurologic disorders	Cerebral palsy (CP) Myelomeningocele Muscular dystrophy
Malignancy	Leukemia Osteoid osteoma Osteosarcoma

22.3 Abnormal Gait

The normal gait cycle is altered by pain, mechanical abnormalities, and neuromuscular disorders. An antalgic gait occurs when stance phase is shortened and is commonly seen when a child is attempting to decrease pain in a limb. The stride length (swing phase) of the uninvolved limb is shortened in order to decrease time spent in single-leg stance on the painful side [2]. In extreme cases, a child may refuse to walk altogether because pain cannot be avoided even with an antalgic gait.

There are several abnormal gait patterns that can be seen in cases where a child may or may not report pain. These gait patterns are associated with biomechanical or neuromuscular aberrations. A Trendelenburg gait is seen when the pelvis drops away from the limb that is in stance phase. Alternatively, a child may lean the trunk over the limb in stance phase to transfer the center of gravity more directly over that limb. A Trendelenburg gait is seen in cases of altered hip mechanics, particularly when abductor weakness is present [2]. A vaulting gait is seen in children with a significant leg length discrepancy in which a child will vault off the short limb in

order to clear the ground with the longer leg [9]. Alternatively, a child with a leg length inequality may toe walk on the short side [2, 9]. A toe-walking gait may also be seen in cases of gastrocnemius and/or soleus tightness or spasticity, Achilles tendon shortening, or ankle joint contracture. In these cases, adequate ankle dorsiflexion cannot be obtained, and therefore initial contact is made with the forefoot rather than the heel. In cases of joint stiffness, a child may walk with a circumduction gait in which there is increased hip abduction, hip hiking, and pelvic rotation during swing phase to functionally shorten the involved limb to allow foot clearance. Gait patterns associated with neuromuscular conditions include the "steppage" or "slapping" gait and ataxic gait. In a steppage gait, a child increases hip and knee flexion during swing phase in order to clear the foot with the foot slapping the ground at contact. This gait pattern is due to weakness in the ankle dorsiflexors, or "drop foot". An ataxic gait is unsteady and results from conditions that negatively affect balance. Finally, a "cautious" gait is seen in children with back pain and shows loss of the normal flexion and extension movements in the lumbar spine that are typically seen during gait.

22.4 Evaluation of the Limping Child

22.4.1 History

A thorough history is a vital component in the workup of a limping child [2, 10–12]. A child may be able to describe symptoms to some degree, but particularly with younger children, parents, grandparents, or primary caregivers are important in obtaining an accurate history. History of recent illness or trauma is helpful. Additionally, the family should be asked about the child's development as failure to achieve developmental milestones may point to a neuromuscular or metabolic condition. In posing additional questions, the physician should ask about the presence or absence of pain, the frequency and duration of symptoms, and the onset of the limp. If a child has chosen to skip free play or sports participation, it should raise concern for a more severe condition [13]. In cases of a painless limp, one should consider neuromuscular, metabolic, and mechanical variations.

The onset, duration, and frequency of pain can be an important component in determining the potential severity. An acute onset and more severe pain points to trauma, infection, or malignancy as potential causes. Malignancy and infection are suspected in cases where pain is constant. Systemic inflammatory conditions and mechanical alterations more likely result in pain that worsens gradually over several weeks to months. Referred pain should be considered as hip conditions can present as knee pain in a child [2, 11, 12, 14].

The timing of pain can also provide clues to the etiology of a child's limp. For example, pain occurring in the morning or after periods of rest is characteristic of inflammatory conditions, whereas activity-associated pain is common when there is a mechanical source of the limp or in cases of overuse injury. Night pain that awakens a child from sleep should raise concern for malignancy [15].

22.4.2 Physical Exam

The physical exam of a limping child consists of a gait exam, standing exam, and bench exam. The physical exam should be performed with the child as exposed as is reasonable since subtle findings can be missed when a child is wearing a large gown or heavy clothing.

The gait exam is crucial and should be performed in an area large enough to see several gait cycles. Watching a child as he or she initially walks into the room is valuable as it allows one to observe the child's gait. A systematic approach, evaluating the foot and ankle, knee, hip, trunk, and upper extremities, can help break a complex movement into more simple components. One should watch how the foot contacts the floor – with the heel versus the forefoot, with weight on the lateral foot or medial foot, and with feet directed inward or outward. Abnormalities in the

frontal plane, such as a varus thrust at the knee, should be noted. Heel walking or toe walking can show subtle weakness in the dorsiflexors or plantarflexors. Finally, running in addition to walking should be observed when possible, as running may accentuate a gait abnormality. In neuromuscular conditions like cerebral palsy, upper extremity posturing may only be apparent during running.

A standing exam is helpful in assessing spinal conditions, leg length inequality, and abductor weakness. Pelvic obliquity when a child is standing can be the result of lumbar scoliosis or a leg length inequality. Shoulder asymmetry is seen with thoracic scoliosis. One should note rib and/or lumbar prominences with forward bending. Cutaneous findings such as café-au-lait spots or sacral dimpling should be noted. Spinal motion can be assessed on standing exam. Additionally, the Trendelenburg test should be performed. With this test, a child is asked to stand on the affected leg with the knee slightly flexed and the hip extended. If the contralateral side of the pelvis drops or the trunk leans over the affected leg, this suggests abductor weakness [16, 17] (Fig. 22.1a, b). Finally, in cases of suspected muscular dystrophy, a child should be asked to rise from a seated position on the floor, looking for a Gower sign, when the child uses the arms to push him up as compensation for weakness in the hip extensors.

After gait and standing exams, the child should be evaluated on the exam table. Physicians should make note of any asymmetry, atrophy/hypertrophy, swelling, erythema, rash, ecchymosis, or wounds. The resting position of the limb can give clues about the location of pathology. In septic arthritis of the hip, a child will hold the hip flexed and externally rotated, while in septic arthritis of the knee, the knee will be held in

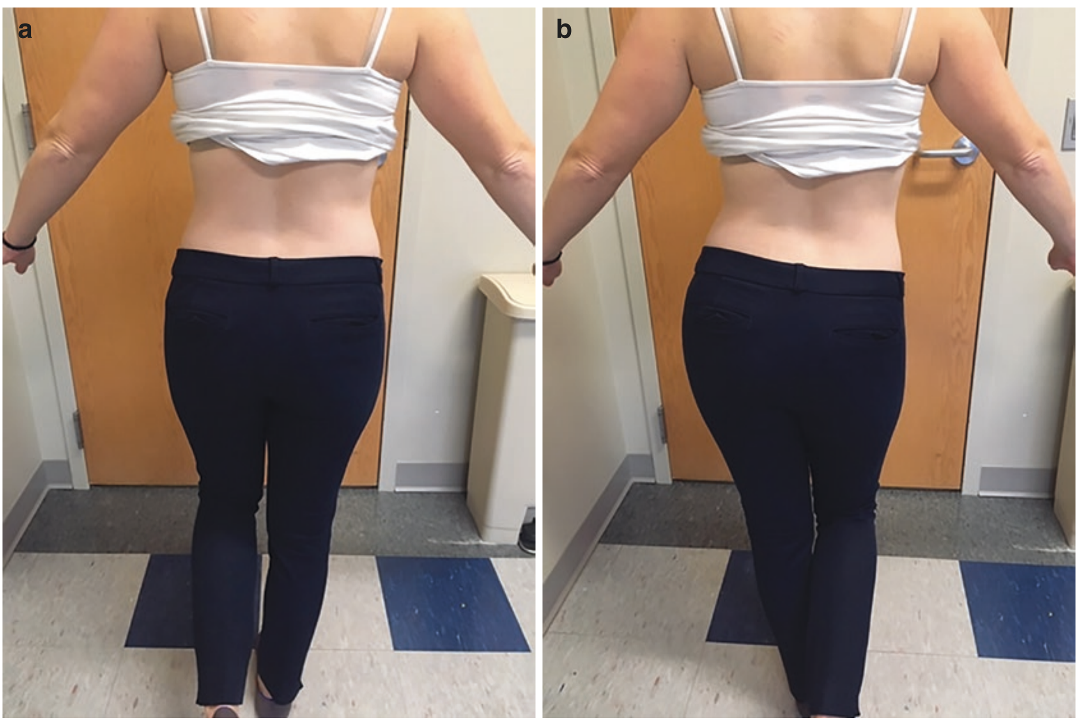

Fig. 22.1 (**a**) The pelvis is level when the patient stands with weight the right leg. (**b**) A positive Trendelenburg sign is seen when the patient stands with weight on the left leg and the right hemipelvis drops

Fig. 22.2 A child with a septic hip will hold the hip in flexion, abduction, and external rotation

Fig. 22.3 A FABER test

mid-flexion (Fig. 22.2). The hip, knee, patellofemoral joint, and ankle should all be taken through their range of motion, and the lower extremity should be palpated to localize the site of maximal pain and tenderness. As the joints are ranged, make note of contractures and spasticity. The sacroiliac joints can be stressed with maximal flexion, abduction, and external rotation of the ipsilateral hip, or FABER test (Fig. 22.3). The Galeazzi test is performed with the child supine, flexing the hips and knees (Fig. 22.4). A leg length discrepancy is suggested if one knee is lower than the other knee. The rotational profile is assessed with the child lying prone, evaluating the thigh-foot angle, which assesses tibial torsion and hip rotation, which is a measurement of femoral version (Fig. 22.5).

22.4.3 Age Considerations

The potential causes for a limp in a child do vary by the age of the child (Table 22.2). Evaluating the

Fig. 22.4 Galeazzi sign

Fig. 22.5 With a patient lying prone, a rotational profile can be obtained and hip (**a**) internal rotation and (**b**) external rotation can be measured

Table 22.2 Causes of limping based on age

Painless limp		Painful limp	
1–3 years	Developmental dysplasia of the hip (DDH) Leg length discrepancy (LLD) Coxa vara Neuromuscular disorder	1–3 years	Injury/trauma Infection Malignancy
4–10 years	Developmental dysplasia of the hip (DDH) Leg length discrepancy (LLD) Coxa vara Neuromuscular disorder	4–10 years	Injury/trauma Infection/inflammatory condition Legg-Calve-Perthes (LCP) Discoid meniscus Malignancy
11–18 years	Developmental dysplasia of the hip (DDH) Leg length discrepancy (LLD) Neuromuscular disorder	11–18 years	Injury/trauma Infection/inflammatory condition Legg-Calve-Perthes (LCP) Slipped capital femoral epiphysis (SCFE) Osteochondritis dissecans (OCD) Malignancy

reason for a limp in a toddler (1–3 years) is difficult as he or she is unable to provide a history and parents may not remember potential injuries. Additionally, fear and anxiety in toddlers can make the physical exam challenging; therefore beginning the exam with the less intimidating tests and including parents in the exam can be helpful. In slightly older children (4–10 years) and adolescents (11–15 years), evaluating a limp is easier due to the improved communication [2]. Additionally, the more mature gait pattern of these children makes variations in gait more noticeable [2].

22.4.4 Laboratory Evaluation

In cases of suspected infection, inflammatory condition, or neoplasm, a complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) should be obtained. If the child is febrile, blood cultures should be obtained as well. In cases of joint effusion and suspected septic arthritis, joint aspiration should be performed and the fluid sent for cell count, gram stain, and culture [18].

22.4.5 Imaging

Diagnostic imaging of a child with a limp should begin with plain radiographs of the suspected region based on physical exam findings [10–12, 14]. In younger children and cases where pain is poorly localized, radiographs of the pelvis, femur, and tibia may be necessary. In cases of potential septic arthritis of the hip, ultrasound can be used to determine if there is a hip effusion and then to guide joint aspiration if needed. In some centers, quick MRI may be available and can be considered as an alternative to ultrasound in cases where there is concern for peripelvic infection. Magnetic resonance imaging (MRI) with contrast is used in cases of suspected osteomyelitis or malignancy.

22.5 Toddler's Fracture

A toddler's fracture is a nondisplaced spiral fracture of the mid to distal tibial shaft that occurs in walking toddlers. It typically is the result of a low energy injury with a rotational component. For example, a parent may describe the child's foot catching on the side of a slide while going down the slide. Children with a toddler's fracture may have minimal swelling and will not have an obvious deformity of the limb. Most commonly the child refuses to bear weight on the involved leg. Physical exam will show tenderness over the tibia, particularly the distal tibia. The child may have pain with ankle motion. Imaging should include AP and lateral radiographs of the involved tibia that include the knee and ankle. Radiographs will show a spiral distal tibia fracture with an intact fibula though some may be radio-occult [19] (Fig. 22.6). Treatment consists of immobilization with a boot or cast most commonly, typically not requiring a formal closed reduction. In cases of a radio-occult fracture, observation alone may be considered.

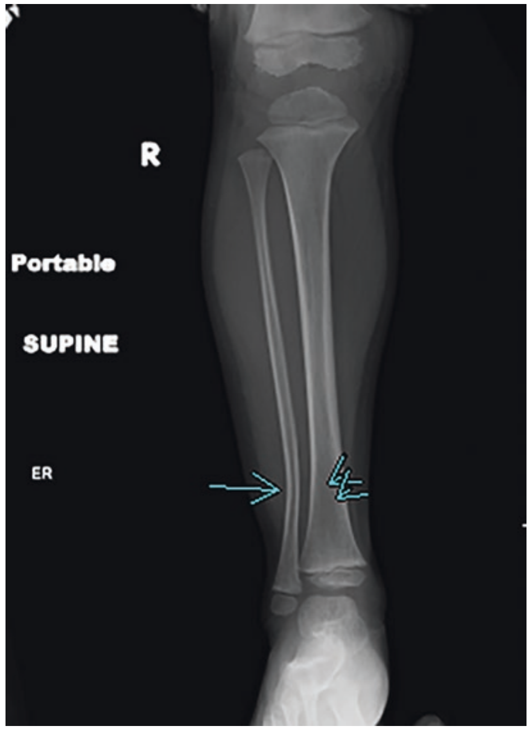

Fig. 22.6 AP radiograph of the right tibia in a 3-year-old child. There is a nondisplaced fracture of the distal tibia (arrowheads) as well as plastic deformity in the fibula (arrow)

22.6 Developmental Dysplasia of the Hip (DDH)

Developmental dysplasia of the hip (DDH) is a condition of abnormal development of the hip ranging from a completely dislocated hip in an infant to a shallow acetabulum in an adult. The term "developmental dysplasia" replaced "congenital dysplasia" because the structures of the hip are normal initially [20]. Over time, dysplasia develops due to laxity and abnormal positioning in utero [20, 21].

DDH is the most common orthopedic condition in infants [20, 22–24]. Risk factors for DDH include female gender, breech presentation at any point during gestation, family history, and oligohydramnios [20, 21, 23, 25, 26]. Screening for DDH in infants is part of the standard newborn exam in order to initiate treatment and prevent missed diagnosis [20, 22, 25–27]. In the infant, the hip may rest in a dislocated position or it may rest located but the capsule and ligaments may be loose enough to allow the hip to subluxate or dislocate. The Barlow and Ortolani maneuvers are used to feel for a located hip that can be dislocated (Barlow positive) or a dislocated hip that can be reduced (Ortolani positive). These maneuvers are helpful during the first 3 months after birth but become less useful in older children.

22.6.1 Presentation

In cases of delayed diagnosis of DDH, a toddler will present with a painless limp. When the hip dislocation is unilateral, the child will walk with a gait consistent with a leg length discrepancy because the dislocated hip causes shortening of the affected extremity. Children with unilateral hip dislocation will be seen toe walking on the affected side or vaulting off the affected leg. Upon standing exam, the child with unilateral involvement will stand with the contralateral knee flexed and have pelvic obliquity when standing with both knees straight. During supine exam, the child will have a positive Galeazzi sign (with hips and knees both flexed, the affected knee will appear lower than the contralateral side). The child may have asymmetric skin folds around the buttock and proximal thigh. Range of motion does not cause pain though the involved hip may show decreased abduction.

A child of walking age with bilateral dislocated hips can be a little more challenging to diagnose. These children have exaggerated lordosis of the lumbar spine and a waddling gait [20, 22, 23, 28–32]. They typically do not complain of pain, and range of motion is not overtly limited as there is bilateral involvement. The child will not have the leg length discrepancy seen in cases of unilateral dislocations. The Klisic sign is helpful in diagnosing bilateral DDH in the toddler or older child (Fig. 22.7). The long fingers are placed on the greater trochanters, and the index fingers are placed on the anterior superior iliac spines (ASIS). If a line were drawn connecting the two, that line should pass through or above the umbilicus. A child with bilateral hip dislocations will have a positive Klisic sign with the line between the greater trochanter and ASIS passing below the umbilicus, indicating high riding greater trochanters seen in cases of hip dislocation.

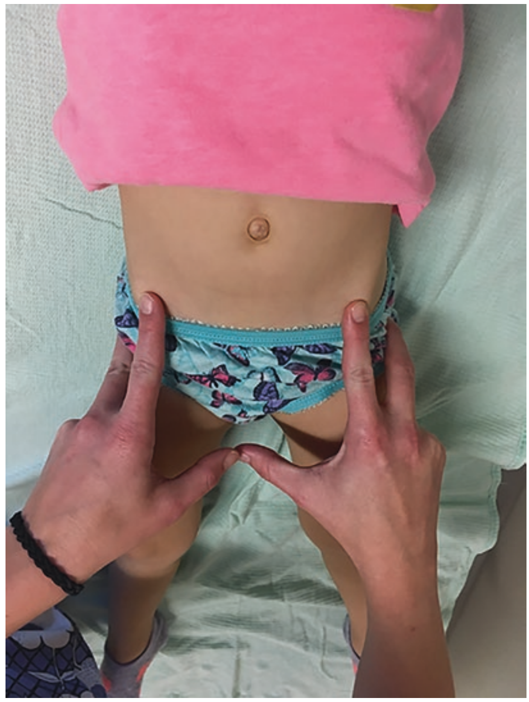

Fig. 22.7 In a toddler with located hips, a line drawn between the long and index fingers will pass through or above the umbilicus

22.6.2 Imaging

In cases of clinical suspicion for hip dislocation in the child, various imaging techniques are used depending on the age of the child. In children <4–6 months, ultrasound is the imaging method of choice as the femoral head ossific nucleus is not yet visible on radiographs [33–37]. Conversely, plain radiography is the imaging modality of choice in children >4–6 months of age. An AP pelvis radiograph can be used to confirm the diagnosis (Fig. 22.8).

Fig. 22.8 AP pelvis radiograph of a 12-month-old child showing a left hip dislocation

22.6.3 Treatment

Infants with an abnormal exam or hip ultrasound are treated with a Pavlik harness with a goal of reducing the dislocation and stabilizing the hip. Children older than 6 months or those who fail treatment with a Pavlik harness are treated with closed reduction of the hip and spica casting in the operating room. Treatment of a dislocated hip in a walking-aged child is typically still aimed at reducing the hip and maintaining the reduction. By 12–18 months of age, this often requires an open rather than closed reduction of the hip. Osteotomies of the acetabulum and/or femur may also be required depending on the age of the patient. In cases of complete dislocations in older children (>6–8 years), results of surgical reduction of the hip are generally poor, particularly in cases of bilateral dislocations [20, 23, 32]. Therefore, these hips may be left untreated.

22.6.4 Complications

There are two feared complications with DDH: missed diagnosis and avascular necrosis (AVN). Avascular necrosis is associated with forceful abduction either during initial treatment in a Pavlik harness or during cast immobilization following closed reduction [38–40]. AVN can also be seen after open reduction or in cases of revision surgery [38–40]. Osteoarthritis is associated with persistent acetabular dysplasia; therefore continued radiographic follow-up until skeletal maturity is recommended [41–43].

22.7 Legg-Calve-Perthes Disease (Juvenile Osteonecrosis of the Femoral Head)

Legg-Calve-Perthes (LCP) disease is an idiopathic avascular necrosis of the proximal femoral epiphysis unique to children. The etiology of LCP is not fully understood, but it does involve a disruption in the blood supply of the femoral head. Typically it is unilateral but when it is bilateral, it is asymmetric. Cases of bilateral, symmetric epiphyseal changes should raise suspicion for a skeletal dysplasia like multiple epiphyseal dysplasia. LCP is a cause of limping in children 4 to 8 years of age and is seen more commonly in males than females (5:1 ratio) [44]. LCP is more common among Caucasians than African Americans [45–48]. Coagulopathy is found in up to 75% of patients with LCP and bone age is delayed in 89% of these patients [45, 46, 49].

LCP is considered a self-limiting process in that there is an initial ischemic event followed by a variable course in healing [45, 46, 48, 49]. The process can take 2–5 years to fully resolve. During healing, LCP progresses through four stages: initial, fragmentation, reossification, and remodeling. These stages are summarized in the Table 22.3.

Table 22.3 Stages of Legg-Calve-Perthes

Initial	Ischemia leads to sclerosis of the epiphysis, widening of the medial joint space	Radiographic findings may lag behind ischemic event up to 6 months
Fragmentation	Subchondral lucency first appears leading to fragmentation of the femoral head due to resorption of bone	Typical stage of presentation due to hip symptoms Lateral pillar classification is based on this stage
Reossification	Femoral head reossifies	Hip symptoms often resolved
Remodeling	Femoral head remodels	Lasts until skeletal maturity

22.7.1 Presentation

Legg-Calve-Perthes often presents with an insidious onset of a limp, either painless or with intermittent complaints of hip, groin, thigh, or knee pain. Physical exam may show stiffness of the affected hip, usually in abduction. Patients may walk with a trendelenburg gait or if painful enough, an antalgic gait.

22.7.2 Imaging

Plain radiographs are critical to the diagnosis of LCP in children and should include an AP pelvis radiograph and frog laterals of the hips [50]. The Lateral Pillar Classification (Table 22.4) is based on the radiographic appearance of the hip at the start of the fragmentation stage [46, 48, 51, 52]. The earliest finding on radiographs is widening of the medial joint space because of loss of ossification of the femoral head. The femoral head may look small and sclerotic early if seen while in the initial stage, or may show subchondral lucency (the "crescent sign") early in the fragmentation stage (Fig. 22.9). Magnetic resonance imaging (MRI) can show signs of epiphyseal and physeal abnormalities before changes are seen on radiographs and may be helpful with the diagnosis very early in the condition [50, 53, 54]. A bone scan can be used to confirm the diagnosis when it is not clear and will show decreased uptake in the femoral head indicating loss of blood supply to the femoral head [50, 55, 56].

Table 22.4 Lateral Pillar Classification of Legg-Calve-Perthes

Group A	Lateral pillar maintains 100% of its height	Consistently do well regardless of age
Group B	Lateral pillar maintains >50% of its height	May do ok when bone age <6 years Prognosis improves with surgery when bone age >6 years
Group B/C	Lateral pillar has ½ of its height	Prognosis improves with surgery when bone age >6 years
Group C	Lateral pillar has <50% of its height	Poor outcomes regardless of age

Fig. 22.9 AP pelvis radiograph of a child with left hip Legg-Calve-Perthes disease. Notice the left femoral epiphysis is shortened, sclerotic, and irregular

The bone scan study can provide information about the extent of femoral head involvement.

22.7.3 Treatment

Treatment of LCP is dependent on patient age and the extent of femoral head involvement. General goals of treatment are to manage symptoms, maintain range of motion of the hip, and maintain acetabular coverage of the femoral head, often termed "containment". Younger children and those with minimal head involvement are treated with initial modification in weight bearing and avoidance of impact activities during the initial and fragmentation phases [45, 46, 49, 57]. Sometimes physical therapy and/or hip abduction bracing or casting is used to help maintain hip motion [58]. Older children and children with greater involvement may be candidates for surgery which aims at increasing coverage or "containment" of the femoral head [45, 46, 49, 57].

22.7.4 Complications

The most notable complication of LCP is deformity of the femoral head. The typical deformity is a flattened, enlarged, and ovoid femoral head. The

flattening of the femoral head and abnormal physeal growth leads to relative shortening of the femoral neck and overgrowth of the greater trochanter apophysis. In this case, a child will walk with a Trendelenburg gait due to shortening of the abductors and may demonstrate a leg length discrepancy. Acetabular dysplasia and lateral subluxation of the femoral head are late consequences that are associated with a poor prognosis.

22.8 Coxa Vara

Coxa vara occurs secondary to a defect in ossification of the inferior portion of the femoral neck. The result is a decreased femoral neck-shaft angle producing a varus femoral neck. The proximal femoral physis becomes vertically oriented and is subsequently subject to increased shear stress (Fig. 22.10).

22.8.1 Presentation

A child with coxa vara is typically evaluated for a gait abnormality. Most children present by 6 years of age and demonstrate a painless waddling or Trendelenburg gait from relative shortening of the abductors that occurs because of the varus femoral neck-shaft angle [59]. On exam, there may be a noticeable leg length discrepancy in cases of unilateral coxa vara. The greater trochanter on the involved side will be highriding. Range of motion is not painful but shows some restriction because of the varus deformity of the proximal femur.

Fig. 22.10 AP radiograph of the right hip showing a vertically oriented proximal femoral physis with the classic "inverted Y" appearance due to defects in ossification of the medial femoral neck

22.8.2 Imaging

Plain radiographs are the key to diagnosis. AP and lateral hip radiographs are performed. The angle between the femoral neck and femoral shaft (femoral neck-shaft angle) is used to confirm coxa vara. Additionally, the physis of the proximal femur will be oriented more vertically. The femoral neck is shortened and the greater trochanter is highriding. A unique finding is a small, triangular fragment of metaphyseal bone along the inferior femoral neck. Additional imaging is not required for the diagnosis, but computed tomography (CT) can be helpful in surgical planning.

22.8.3 Treatment

Treatment of coxa vara is dependent on the severity of the deformity. With increased varus angle of the femoral neck, the physis becomes more vertically oriented. It is actually the relative verticality of the physis that determines need for surgery to reorient the proximal femur and reduce the shear stress through the physis [59, 60].

22.9 Slipped Capital Femoral Epiphysis (SCFE)

Slipped capital femoral epiphysis (SCFE) is the most common hip disorder affecting adolescents. During periods of rapid growth, increased shear stress of the hypertrophic zone of the proximal femoral physis results in displacement of the epiphysis relative to the metaphysis. In reality, the epiphysis actually maintains its position in the acetabulum, while the metaphysis displaces anteriorly and proximally such that the epiphysis lies posterior to the femoral neck. Additionally, the metaphysis externally rotates as it displaces [61].

SCFE occurs more commonly in males than females and is particularly common in obese adolescents. As the prevalence of obesity among children and adolescents has increased, so too has the incidence of SFCE. Similarly, the average age at which SCFE is diagnosed has also decreased [62]. Bilateral involvement is reported in 20–40% of cases. A particularly high prevalence of SCFE is seen among Pacific islanders and African Americans [63]. Though it is most common in adolescents (girls 11–13 years and boys 12–15 years), SCFE can be found in younger children with the youngest reported case of SCFE in a patient without an endocrinopathy being 5 years 9 months [64, 65]. Cases of SCFE in children <10 years of age should raise concern for an endocrine or metabolic abnormality, most commonly hypothyroidism, growth hormone deficiency, or chronic renal disease [66]. These young children are at high risk of a contralateral slip, usually occurring within 14–18 months after the initial slip [62, 66, 67].

Fig. 22.11 This patient has obligate external rotation in which the hip externally rotates as it is brought into a flexed position

22.9.1 Classification

SCFE is most commonly classified as unstable or stable depending on whether a child is able to walk. A stable slip occurs when a child is able to walk either with or without crutches, bearing all or some weight [68]. An unstable slip occurs when a child is not able to walk, even with the use of crutches [68]. This classification system is favored as it is correlated with the risk of developing avascular necrosis (AVN). AVN has been reported in 10–47% of hips following an unstable SCFE [67, 69–74].

22.9.2 Presentation

Typically, a child or adolescent with a slipped capital femoral epiphysis will report vague pain in the affected extremity. Pain may be located in either the hip or proximal thigh. Alternatively, a child may complain only of knee pain [75]. Clinically, children have an antalgic or waddling gait with the affected leg externally rotated. Physical exam will show decreased hip motion, particularly flexion and internal rotation. Obligatory external rotation of the hip while bringing it into a flexed position is a hallmark sign of SCFE (Fig. 22.11).

22.9.3 Imaging

An AP pelvis and lateral radiograph of the hips will diagnose SCFE (Fig. 22.12). When possible a frog-lateral radiograph is most helpful but in cases of unstable SCFE it may be too painful to obtain this view. In this case, a cross-table lateral radiograph of the hip may be more appropriate.

Early x-ray findings include widening of the physis. As a slip progresses, the AP view will show overlap of the epiphysis and metaphysis and shortening of the epiphysis. The severity of the slip can be seen on the lateral view. Magnetic resonance imaging (MRI), while typically not necessary to diagnose SCFE, can be helpful in diagnosing a pre-slip

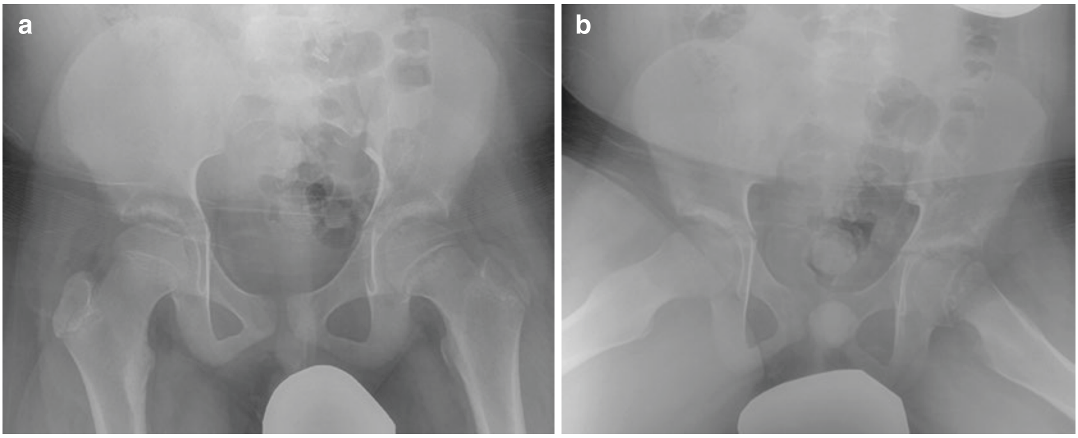

Fig. 22.12 AP pelvis and frog lateral views of the hips in a 12-year-old girl. (**a**) There is widening of the left proximal femoral physis. (**b**) The frog lateral view more clearly shows the left slipped capital femoral epiphysis

condition in which case the MRI will show widening of the physis and edema in the metaphysis.

22.9.4 Treatment

The treatment of SCFE is aimed at stabilizing the proximal femoral physis in order to prevent further slip. There is controversy as to whether or not to reduce the displacement as high rates of AVN have been found with reduction of the slip. The most common procedure performed is in situ pinning of the slip (Fig. 22.13). This is the treatment of choice for stable SCFE. With in situ pinning, a cannulated screw is placed across the physis to prevent further slipping. The goal is to position the screw in the center of the femoral head and short of the subchondral bone to prevent screw penetration of the joint and subsequent chondrolysis.

Fig. 22.13 Radiograph showing a right hip following in situ pinning of a SCFE

22.9.5 Complications

The most severe complication following SCFE is avascular necrosis (AVN) of the femoral head. AVN is a result of damage to the blood supply by acute displacement though it can result from damage to blood supply during a reduction maneuver if one is attempted. Other complications include progression of the slip despite screw fixation, contralateral slip, chondrolysis, hip stiffness, hip impingement secondary to the proximal femoral deformity, and arthritis.

22.10 Osteomyelitis, Septic Arthritis, Discitis

Osteomyelitis is defined as acute infection of the bone. In children, it occurs most commonly by hematogenous seeding. Children are more prone to acute and subacute osteomyelitis because of the vast metaphyseal blood supply and immature immune system. Metaphyseal blood flow slows as it passes through tight turns at the level of the physis. Combined with the low oxygen tension and acidic pH near the physis, bacterial seeding and growth can easily occur. As the immune system targets bacteria, inflammatory mediators are released resulting in osteoblast death and osteoclast activation. The result is purulence and increasing pressure within the medullary canal of the bone. Abscess can form beneath the periosteum, known as a subperiosteal abscess. Septic arthritis can occur when osteomyelitis is present around a joint with an intra-articular physis such as the shoulder, hip, elbow, or ankle. In children under 1 year of age, capillaries cross the physis; therefore osteomyelitis can commonly result in septic arthritis regardless of physeal location relative to the joint.

Septic arthritis occurs when there is an intra-articular infection. Septic arthritis in a child is a surgical emergency and requires prompt recognition in order to initiate treatment. Septic arthritis is most common in young children, with half of cases in kids under 2 years of age. The hip and knee joints are more commonly involved. Septic arthritis occurs most commonly from hematogenous seeding or extension from osteomyelitis in newborns or around the hip, shoulder, elbow, or ankle in older children. The release of matrix metalloproteinases in response to infection results in articular cartilage damage. In the hip, the increased pressure in the joint may cause osteonecrosis of the femoral head.

Discitis, or infection of the disc space, is more common in children than adults [76]. It occurs because the blood vessels in children extend from the end plate of the vertebral body to the nucleus pulposus of the disc, resulting in direct inoculation of the disc. It most commonly affects the lumbar spine [76].

22.10.1 Presentation

Children with acute osteomyelitis or septic arthritis will present with a painful limp or refusal to bear weight on the affected limb. With discitis, children will walk with a stiff gait, trying to avoid trunk motion. Toddlers with discitis may refuse to walk. There may be a history of recent infection or trauma to the area. Children may or may not have a fever in cases of osteomyelitis or discitis depending on if it is acute, subacute, or a more chronic infection. In septic arthritis, systemic symptoms are common except in neonates due to their inability to mount a strong immune response. With discitis, there is commonly a complaint of abdominal pain and loss of appetite [76]. On exam, the affected area may be swollen and erythematous. With septic arthritis, there is a joint effusion. The child will have tenderness over the involved area with all conditions. Motion of the extremity may be limited by pain, particularly in cases of septic arthritis. A child with a septic hip will hold the hip flexed, abducted, and externally rotated as this position maximally opens the joint space (Fig. 22.2).

22.10.2 Imaging

AP and lateral radiographs of the affected area should be obtained first. Early on in cases of acute osteomyelitis, there will not likely be bony changes but just soft tissue swelling. After about 1 week, periosteal new bone formation can be seen and after 2 weeks, osteolysis is evident. Radiographs in septic arthritis will show a joint effusion. Hip radiographs will show joint widening and may show subluxation or dislocation of the femoral head. Loss of lumbar lordosis is often the earliest radiographic finding in discitis. Two to 3 weeks after the start of the infection, radiographs begin to show erosion of the end plates and disc space narrowing of the involved levels.

Hip ultrasound can identify a hip effusion and can be used to guide hip joint aspiration.

Magnetic resonance imaging (MRI) utilizing intravenous contrast has become a common imaging modality to assess for subperiosteal

abscess, surrounding intramuscular abscess and myositis, and is the diagnostic test of choice in cases of diskitis [77]. In young children, a full MRI typically requires sedation or anesthesia and depending on the medical center, this may or may not be readily available during inital evaluation. At some institutions, a "quick MRI" is available for evaluation of infection around the pelvis without the need for anesthesia, however this is a newer technique. In cases of septic arthritis, MRI may be used if a child is not responding to intravenous antibiotics after surgical drainage. With osteomyelitis, an MRI will show hyperintense T2 signal within the medullary canal and contrast enhancement of any existing abscess. Bone scan can also be used to localize an infection in the cast of normal radiographs and a non-focal exam.

22.10.3 Lab Studies

A complete blood count (CBC) with differential, sedimentation rate (ESR), and C-reactive protein (CRP) should be obtained in cases of suspected infection. The white blood cell count (WBC) is increased in only about 25% of children with osteomyelitis. In contrast, CRP and ESR are elevated in at least 90% of patients. The CRP becomes elevated within 6 hours and declines rapidly making it an ideal lab study to monitor response to treatment. ESR peaks 3–5 days into an infection and takes longer to normalize. ESR is not a reliable study in neonates however, due to their immature immune response. Blood cultures should be drawn prior to any antibiotic administration.

In cases of septic arthritis, joint aspiration is performed to obtain fluid. The fluid should be sent for cell count, gram stain, and culture. Synovial fluid cell count >50,000 nucleated cells/mm3 with >75% PMNs is indicative of infection. For septic arthritis of the hip, the Kocher Criteria, have been used to assess the likelihood of septic arthritis [78–80] (Table 22.5). More recently, CRP > 2.0 mg/dL has been shown to be an independent predictor of septic arthritis and when combined with fever, the likelihood of septic arthritis is 74% [81].

Table 22.5 Kocher Criteria for predicting the likelihood of septic arthritis of the hip

Serum WBC > 12,000 cells/microL	1 criteria = 3%
Fever >101.3 °F (38.5 °C)	2 criteria = 40%
ESR > 40 mm/hr	3 criteria = 93%
Inability to bear weight	All 4 criteria = 99.6%

Table 22.6 Most common causes of septic arthritis and osteomyelitis in children

<12 months	*Staphylococcus* species Group B Strep Gram-negative bacilli
6 months to 5 years	*Staphylococcus aureus* *Streptococcus pneumoniae* *Kingella kingae* *H. influenzae*
5–12 years	*Staphylococcus aureus* *Kingella kingae*
12–18 years	*Neisseria gonorrhoeae* *Staphylococcus aureus*
Children with sickle cell anemia	*Salmonella*

In cases of osteomyelitis, blood cultures can be used to guide antibiotic therapy. When blood cultures are negative, empiric therapy targeting the most common causes of osteomyelitis may be started. *Staphylococcus aureus* is the most common bacterial pathogen with *Streptococcus* species following. Bone aspiration or bone biopsy and culture can also be done to help establish the diagnosis. Common bacterial pathogens in septic arthritis and osteomyelitis are presented in Table 22.6.

22.10.4 Treatment

Acute osteomyelitis in children is primarily treated with antibiotics alone. Generally children are started on intravenous antibiotics. There has been a more recent push to transition children to oral antibiotics more quickly in treatment once inflammatory markers have normalized [82]. In cases of subperiosteal or intramedullary abscess, surgery is indicated to drain the fluid collection. Surgery is also indicated for children who do not respond to appro-

priate antibiotic therapy. Any operative cultures should be sent for culture and pathology review.

For septic arthritis, emergent surgical joint drainage and debridement with antibiotic treatment after cultures have been obtained is the standard of care [78, 82, 83]. Again, treatment is started with intravenous antibiotics and children are transitioned to oral antibiotics with normalization of inflammatory markers.

Discitis can usually be treated nonoperatively with bed rest, bracing to immobilize the spine and appropriate antibiotic therapy. Labs are followed to monitor efficacy of treatment. In cases of poor response to nonoperative treatment, paraspinal abscess, or late infection, surgery is indicated [77].

22.10.5 Complications

Osteomyelitis weakens the affected bone temporarily due to the osteoblast necrosis and increased osteoclast activity [84]. As a result, fracture can occur in the infected and acutely recovering bone. Septic arthritis can cause irreversible damage to articular cartilage, particularly when diagnosis and appropriate intervention is delayed. With septic arthritis of the hip, a delay in diagnosis can result in elevated intracapsular pressure and subsequent avascular necrosis of the femoral head [78, 80]. Metaphyseal osteomyelitis and septic arthritis of the hip, shoulder, elbow, or ankle (intra-articular physes) can result in growth disturbances secondary to physeal injury. Complications of discitis include permanent disc space narrowing, fusion of vertebral bodies, and chronic back pain. In cases of methicillin-resistant Staphylococcus aureus (MRSA) infection, deep venous thrombosis (DVT) and pulmonary embolism can occur [85]. Risk factors for DVT in the setting of MRSA osteomyelitis include age >8 years, CRP > 6, and surgical treatment [85].

22.11 Transient Synovitis of the Hip

Transient synovitis is the most common reason for hip pain and limp in children [14]. It is found most commonly in children 4–8 years of age [14, 86]. The etiology of transient synovitis is not entirely understood. In transient synovitis, there is aseptic inflammation of the synovium of the hip with a resultant hip effusion.

22.11.1 Presentation

Children with transient synovitis typically complain of hip, groin, or thigh pain. Commonly there is a history of recent viral or bacterial infection [14]. Children are typically afebrile or have only a low-grade fever and otherwise look well. A child may hold the hip flexed, abducted, and externally rotated to take advantage of the position allowing the greatest capsular expansion. There is some restriction to motion particularly with abduction or internal rotation of the hip.

22.11.2 Imaging

Plain radiographs including AP and lateral views of the hip should be obtained first. Typically radiographs will be normal, but in cases where there is a large effusion, there may be widening of the medial joint space. Ultrasound will show a hip joint effusion and may show thickening of the synovium of the joint [87]. If there is concern for infection, ultrasound can be used to guide joint aspiration in order to obtain synovial fluid for analysis. Any additional imaging is not typically necessary to diagnose transient arthritis.

22.11.3 Laboratory Studies

Just as in workup for septic arthritis, a CBC with differential, CRP, and ESR are obtained. The WBC may be normal or just slightly elevated. CRP and ESR are elevated, but CRP usually remains less than 20 mg/L (2.0 mg/dL) and ESR less than 20 mm/h [80, 86].

22.11.4 Treatment

Once the diagnosis of transient arthritis is made, treatment including non-steroidal anti-inflammatory

Table 22.7 Classification of juvenile idiopathic arthritis

Polyarticular (30%)	≥5 joints, small joint involvement, symmetric	Hand and wrist involvement is most common
Pauciarticular (oligoarticular) (50%)	<5 joints, large joints, asymmetric Ocular involvement	Need frequent ophthalmology evaluations Early onset seen more in girls; late onset seen more in boys Most common and best prognosis
Systemic (20%)	Systemic symptoms (rash, fever) Pericarditis and hepatosplenomegaly	Still's disease Poorest prognosis

drugs (NSAIDs) such as ibuprofen, naproxen or toradol can be administered and the patient is observed for improvement in symptoms [14, 86]. Early weight bearing and hip motion are encouraged as pain allows. Symptoms should resolve within a week.

22.12 Juvenile Idiopathic Arthritis (JIA)

Previously termed juvenile rheumatoid arthritis, JIA is an autoimmune inflammatory condition seen in children <16 years of age [88]. In JIA, inflammatory arthritis persists for more than 6 weeks. It most commonly affects the knee but is also seen in the wrist, ankle, hip, and cervical spine [88, 89]. It may affect just one joint, a few joints, or cause systemic inflammation affecting other organ systems (Table 22.7). JIA affects females more often than males and genetic markers of the disease do exist.

22.12.1 Presentation

Children with JIA present with joint effusion, pain, and stiffness. The limp is often the worst in the morning but improves throughout the day. The child may have a low-grade fever as well. The child may or may not report visual changes or rash.

22.12.2 Imaging

Radiographs of the involved joint(s) are usually normal at the time of presentation. Later, osteopenia around the involved joint(s) can be seen on radiographs. Joint destruction is seen as a late finding. Because JIA can affect the synovial joints of the cervical spine (facet joints), it is recommended that children with JIA undergo flexion and extension radiographs of the cervical spine to rule out atlanto-axial instability.

22.12.3 Laboratory Findings

Laboratory workup of JIA includes CBC with differential, ESR, and CRP. Additionally, antinuclear antibody (ANA) levels are drawn. In JIA, RF is usually negative [88, 89]. A positive RF is associated with more severe disease. A positive ANA is used to help diagnose JIA.

22.12.4 Treatment

First-line treatment of JIA consists of disease-modifying anti-rheumatic drugs (DMARDs) just as in rheumatoid arthritis [88, 89].

22.13 Juvenile Osteochondritis Dissecans of the Knee

Osteochondritis dissecans (OCD) of the knee is an acquired lesion of subchondral bone, most commonly affecting the lateral aspect of the medial femoral condyle. The exact etiology is not entirely understood, but hypotheses include altered blood flow and repetitive microtrauma [90]. The incidence of OCD of the knee is rising, likely due to

improved recognition and diagnosis as well as increased participation in organized sports [90].

22.13.1 Presentation

Children and adolescents with OCD of the knee complain of vague, activity-related knee pain. There may or may not be reports of mechanical symptoms like catching, locking, or giving way. Knee effusion following activity may also be reported. Parents often notice the child limps during or after activity. Physical exam may show an antalgic gait. A child may also have a knee effusion. When the knee is maximally flexed, a child often has some tenderness over the involved femoral condyle. When the OCD lesion is in the typical location on the medial femoral condyle, a child may have pain when the tibia is internally rotated while the knee is flexed.

22.13.2 Imaging

To evaluate a child with persistent knee pain, it is necessary to obtain four radiographic views of the knee, including AP, lateral, tunnel, and Merchant views. The tunnel view is vital to diagnosing OCD lesions in the knee as it allows one to see the posterior aspect of the femoral condyles

Fig. 22.15 Coronal T2 MRI of the right knee in a skeletally immature child who has been undergoing nonoperative treatment of medial femoral condyle OCD showing a linear high-intensity T2 signal separating the parent and progeny bone concerning for instability

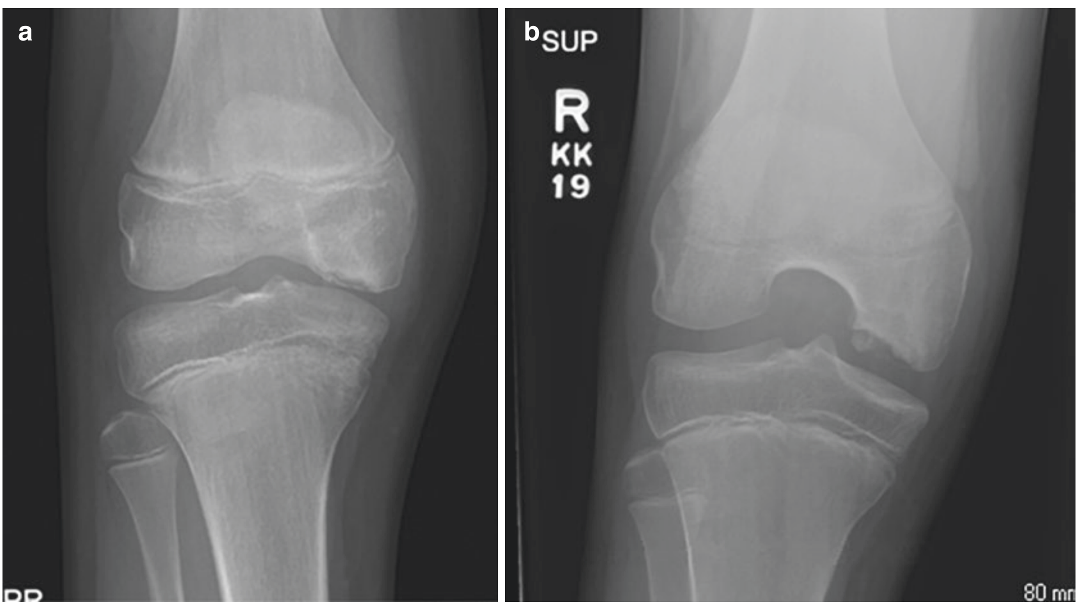

Fig. 22.14 (**a**) AP and (**b**) tunnel radiographs of the right knee in a 12-year-old boy with persistent knee pain. The tunnel view allows for improved visualization of the medial femoral condyle OCD lesion

(Fig. 22.14). In younger children, < 7 years of age, there can be variants in ossification of the femoral condyles that can be confused for OCD so history and physical exam are important aspects to consider when evaluating radiographs. Plain x-rays are also used to assess whether or not a patient's growth plates are still open as skeletal maturity is an important prognostic indicator.

When an OCD lesion is diagnosed on x-ray, MRI is recommended to stage the lesion and guide treatment decisions [90–93]. A linear high intensity T2 signal separating the parent bone (normal epiphyseal bone) from the progeny bone (diseased subchondral bone) of the OCD lesion, multiple or large cyst-like lesions in the bone, and fissuring of the articular cartilage are suggestive of instability and failure of nonoperative treatment (Fig. 22.15). Radiographs and MRI are both used when following an OCD lesion for healing [90, 92–94].

22.13.3 Treatment

Treatment for juvenile OCD of the knee depends on the lesion size, MRI characteristics, and location in addition to the patient's skeletal maturity and symptoms. Nonoperative treatment consisting of a combination of activity modification, weight-bearing restrictions, physical therapy, casting, or bracing is first-line treatment for a stable OCD lesion in a skeletally immature patient [90, 92, 93]. Generally, children are advised to avoid high-impact activities like running or jumping. Surgery is indicated for unstable OCD lesions, stable and unstable OCD lesions in skeletally mature patients, and stable OCD lesions in skeletally immature patients that fail to respond to nonoperative treatment. The goal of surgery is to promote a biological environment for healing and provide stability to the lesion.

22.13.4 Complications

Short-term complications of juvenile osteochondritis dissecans of the knee include failure to heal or the development of loose bodies in the knee should a lesion become unstable and detach. Long-term, the loss of structural support of the articular cartilage that occurs in the setting of juvenile osteochondritis dissecans of the knee can lead to osteoarthritis.

22.14 Discoid Meniscus

Discoid meniscus is a congenital variant, most commonly of the lateral meniscus. In discoid meniscus, there is abnormal meniscal morphology and composition [95]. The result is a larger than typical meniscus that may be unstable and is typically more prone to tearing.

22.14.1 Presentation

Discoid meniscus typically presents as a child with a snapping or popping knee. A child may have a loss of motion in the knee, lacking full knee extension. The child may complain of pain and swelling with activity.

22.14.2 Imaging

Plain radiographs of the knee are obtained first, including AP, lateral, tunnel, and Merchant views of the knee. Subtle radiographic signs of discoid lateral meniscus include flattening of the lateral femoral condyle with a widened lateral joint space. The lateral tibial plateau may be concave. Tunnel views are important to evaluate for co-existing osteochondritis dissecans which can be found in the lateral femoral condyle of individuals with a discoid lateral meniscus.

In the case of a symptomatic discoid meniscus, MRI should follow plain radiographs. On sagittal MRI cuts, there will be a continuous meniscus from the anterior horn to the posterior horn on at least three consecutive sagittal 5 mm cuts [96].

22.14.3 Treatment

In cases of asymptomatic discoid meniscus, observation can be instituted [97]. When there is instability of the discoid meniscus or evidence of

tearing, surgery is recommended to repair and stabilize the meniscus [95]. Typically, the meniscus is also saucerized to remove excess meniscal bulk and give the discoid meniscus a more normal shape.

22.14.4 Complications

Due to the abnormal organization of collagen in a discoid meniscus and instability, discoid menisci are prone to tearing. Children may require multiple procedures, which can lead to near total meniscectomy [95]. In these cases, meniscal transplant is a consideration.

22.15 Tarsal Coalition

A tarsal coalition is an abnormal connection between two otherwise distinct bones in the foot. The abnormal connection can be osseous, cartilaginous, or fibrous. Most commonly these connections are between the anterior process of the calcaneus and the lateral navicular, a calcaneonavicular coalition, or between the talus and the calcaneus, a talocalcaneal coalition. There is a wide range of reported incidence of tarsal coalition, likely because many coalitions are asymptomatic. Tarsal coalition is seen in conjunction with conditions like fibular longitudinal deficiency and proximal femoral focal deficiency (PFFD).

Fig. 22.16 Oblique radiograph of the left foot showing a calcaneonavicular coalition

22.15.1 Presentation

Symptomatic tarsal coalition typically presents in older children and adolescents, 8–13 years of age [98–100]. These children complain of vague lateral foot and sometimes ankle pain. Children with a tarsal coalition tend to have a rigid flat foot, which can be confirmed by asking a child to rise onto his or her toes. Normally, when a child does this, the heels turn inward. In the case of a rigid flatfoot, the heel will be fixed upon heel rise. A child with a coalition may report frequent ankle sprains.

Fig. 22.17 Lateral radiograph of the left ankle showing a "C sign" suggestive of a talocalcaneal coalition

22.15.2 Imaging

Standing plain radiographs are recommended when evaluating a painful, rigid flat foot. Dorsal beaking of the talus is often seen with tarsal coalition. A calcaneonavicular coalition can be seen on a 45° oblique radiograph, showing elongation of the anterior process of the anterior process of the calcaneous or a clear osseous connection between the calcaneus and the navicular (Fig. 22.16). A talocalcaneal coalition may be evident on a lateral radiograph of the foot by the "C sign" but may be better visualized on coronal CT images (Fig. 22.17).

In cases where plain radiographs are not clear or when planning surgery, CT is the standard imaging of choice. CT can show the extent of involvement of the joint, which is important if considering surgery for a talocalcaneal coalition. MRI has been used more recently, but its sensitivity in detecting a coalition is not improved over that of CT.

22.15.3 Treatment

Symptomatic tarsal coalitions are first treated with nonoperative measures, including cast or boot immobilization. Typically the use of an orthosis or arch support follows the period of immobilization. Therapy may or may not be instituted to improve heel cord flexibility.

If symptoms persist despite nonoperative treatment, surgery is reasonable. For a calcaneonavicular coalition, the coalition can be excised. Either local fat or the extensor digitorum brevis (EDB) is interposed between the bone ends to prevent recurrence. In the case of talocalcaneal coalition, surgery is dependent on the degree of joint involvement. Historically, a talocalcaneal coalition comprising more than 50% of the joint was an indication for talocalcaneal fusion rather than excision. More recently, resection has been attempted even in these more involved coalitions with similar long-term outcomes. Some suggest correcting the hindfoot position as management of the symptomatic talocalcaneal coalition [101].

22.15.4 Complications

Persistent pain, recurrence of the coalition, and arthritis of the involved or adjacent joints can occur in the setting of tarsal coalition.

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Common Clinical Conditions of the Spine

23

Daniel L. Robinson

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the common clinical conditions of the spine
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Clinical syndromes affecting the spine
  2. Differences between cervical myelopathy and radiculopathy
  3. Basic workup of lumbosacral radiculopathy
  4. Unique presentation of vascular versus neurogenic claudication
  5. “Red flag symptoms” of vertebral compression fractures
  6. Two major classes of spondylolisthesis
  7. Treatment options for the outlined pathologies

Cervical radiculopathy is a clinic syndrome occurring with impingement or irritation of a nerve root in the cervical spine [1]. Cervical radiculopathy most commonly results from

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degenerative changes of the spine, with contributions from both the bony architecture and soft tissues. As the intervertebral discs degenerate, there is loss of height between adjacent vertebrae and resultant loss of height of the neural foramen. Hypertrophic osteophytes of the uncovertebral and facet joints may impinge upon the exit nerve root. Additionally, the intervertebral disc can herniate posteriorly and impinge on the exiting nerve root. Any combination of these degenerative changes can result in inflammation and ischemia of the nerve radicle, producing the signs and symptoms of cervical radiculopathy [2].

The symptoms of cervical radiculopathy occur in a specific dermatomal pattern. Patients may present with neck pain, radiating arm pain, or both. Pain is typically described as burning or sharp in nature. Additional symptoms include weakness, sensory disturbances, numbness, and tingling in a dermatomal pattern [1]. On physical exam, patients may have diminished reflexes in the corresponding myotomes.

In general, cervical radiculopathy is a self-limited process. A classic study by Lees and Turner observed 44 patients diagnosed with cervical radiculopathy. Patient outcomes were monitored from 3 to 40 years after initial presentation. Forty-five percent of patients at long-term follow-up had a single episode of pain that spontaneously resolved without treatment. An additional 29% had mild or intermittent pain that persisted through long-term follow-up [3]. Another study by Radhakrishnan et al. found that 90% of patients with an initial diagnosis of cervical radiculopathy had no residual symptoms or were minimally affected by their condition 6 years after diagnosis; 26% of these patients underwent surgery [4].

Diagnostic studies for radiculopathy begin with plain radiographs of the cervical spine, which typically demonstrate spondylosis and degenerative changes of the spine. Oblique X-rays can be used to evaluate the neural foramen. Given the self-limited nature of radiculopathy, advanced imaging is typically not obtained unless symptoms persist after 6 weeks of nonoperative treatment unless there are severe or "red flag" symptoms. MRI of the cervical spine is the best imaging study to evaluate soft tissues in the spine and nerve root impingement [5]. MRI additionally allows evaluation of concordant central stenosis and myelomalacia [6]. When MRI is contraindicated or unavailable, a CT myelogram is an alternative advance imaging option.

When evaluating cervical radiculopathy, it is important to assess for "red flag" symptoms or warning signs. As with most spinal pathologies, a history of malignancy, unintentional weight loss, severe nighttime pain, chills, fever, or a history of intravenous drug use warrants more urgent evaluation and imaging. Additionally, progressive weakness or numbness of the upper extremity should warrant expedited workup [7]. Warning signs that would indicate a diagnosis of cervical myelopathy (or myeloradiculopathy) include upper motor neuron signs including hyperreflexia in the lower extremities, pathologic reflexes, balance and gait issues, and difficulty with fine motor movements and hand dexterity.

Initial treatment of cervical radiculopathy is nonoperative in the absence of warning signs. As discussed, radiculopathy is predominantly self-limited, and 90% of patients will have no symptoms or mild, intermittent symptoms at long-term follow-up [4]. Initial nonsurgical treatment consists of oral analgesics including acetaminophen and NSAIDs for pain relief. Steroid tapers may provide relief of symptoms. A brief trial of soft collar immobilization for 1–2 weeks may help pain, although data supporting this is lacking. Physical therapy may provide symptomatic relief and includes multimodal treatment with traction, immobilization, progressive strength training and stretching, ultrasound, massage, and postural and ergonomic training. Physical therapy provides short-term benefits that diminish after 6–12 months. Therapy is solely for symptomatic relief and does not change the natural course of radiculopathy. If patients fail initial nonoperative management, cervical epidural steroid injections can provide good relief of symptoms. One year after epidural injections,

approximately 68% have "good" or "very good" relief of symptoms [5].

There are no well-defined, evidence-based criteria for the surgical treatment of cervical radiculopathy, as the majority of patients will have relief of symptoms with nonoperative management. Surgery is generally indicated when patients fail to improve with an adequate trial nonoperative treatment. Another relative indication for surgery is severe features including progressive muscle weakness or sensory deficits [1, 8]. Choosing the optimal surgical technique for cervical radiculopathy is beyond the scope of this chapter. Briefly, the anterior approach to the spine with anterior cervical decompression and fusion (ACDF) is the workhorse procedure for cervical radiculopathy and involves resection of the intervertebral disc, decompression of the nerve roots, and subsequent fusion of the vertebrae. Cervical disc arthroplasty is an alternative treatment that retains motion of the cervical spine and avoids complications of fusion. Posterior cervical decompression and foraminotomy is rarely necessary but serves as a valuable tool for radiculopathy resulting from posterior pathologies (e.g., foraminal stenosis due to foraminal disc herniation) (Fig. 23.1).

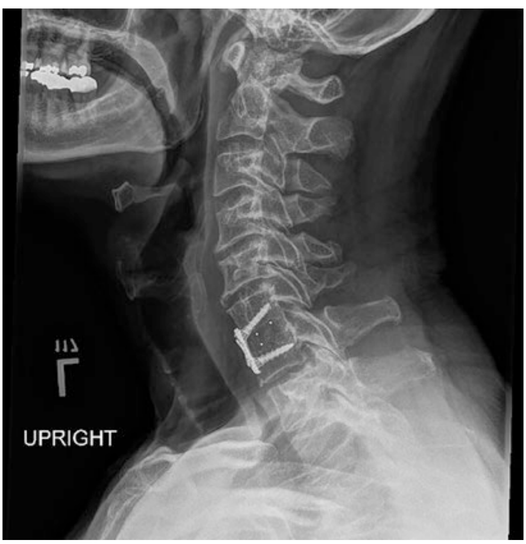

Fig. 23.1 Lateral cervical spine X-ray demonstrating ACDF at C6–7 for recalcitrant cervical radiculopathy

23.1 Cervical and Thoracic Myelopathy

Cervical myelopathy is a clinical syndrome that presents with spinal cord dysfunction resulting from compression of the cord directly or surrounding vasculature [6]. Compression resulting in myelopathy most commonly occurs in the cervical spine but can also occur in the thoracic spine. Myelopathy results from both static and dynamic components. Static factors include spondylosis and degeneration of the bony architecture, bulging of the intervertebral discs, and hypertrophy of the ligamentum flavum. Spondylotic changes cause further instability of the facet joints and, when combined with loss of ligamentous stabilizers, result in dynamic compression of the cord with neck movement. These static and dynamic compressive forces lead to ischemia and inflammation of the cord, cellular injury, and ultimately cell death. Less common etiologies of myelopathy include ossification of the posterior longitudinal ligament or ossification of the ligamentum flavum [9].

Signs and symptoms of myelopathy are highly variable. Patients may present with nonspecific pain in the neck and shoulders occasionally with radiation to the arms (myeloradiculopathy). Myelopathy can cause numbness and tingling in the upper extremities that may or may not be dermatomal. Patients may have symptoms of gait ataxia, balance disturbances, hand clumsiness, and trouble with manual dexterity. Lower extremity symptoms include sensory disturbances and weakness. Physical exam can demonstrate overt weakness, sensory disturbances, and hyperreflexia in both upper and lower extremities. It is important to assess balance and gait; patients may have a positive Romberg sign and unsteadiness during tandem gait. Pathologic reflexes including Hoffman's sign, inverted radial reflex, ankle clonus, and an extensor response with Babinski testing may be elicited in myelopathy [1].

Similar to symptomatology, the natural history of cervical myelopathy varies greatly. In general, it is a progressive process, but disease course can vary immensely between patients. A classic study by Clarke and Robinson followed a

cohort of patients and defined three predominant patterns of myelopathy. Seventy-five percent of patients demonstrated a stepwise decline in neurologic function. They demonstrated long periods of stable symptoms interrupted by discrete episodes of decline. Twenty percent of myelopathic patients had a slow but progressive worsening of symptoms without discrete periods of decline or stability. The remaining 5% demonstrated a more rapid course with unrelenting deterioration of neurologic function [10]. More recent studies demonstrate cervical myelopathy is more heterogenous in nature. Some patients may have long periods of quiescence without neurologic decline nor need for surgical intervention 10 years or more from initial presentation. Others will follow the classic stepwise decline with discrete periods of worsening similar to those described by Clarke and Robinson [11]. While there are different disease courses, it is impossible to know at the initial presentation how an individual will progress. A review article by Fehlings et al. compiling data from multiple studies found that 20–62% with cervical myelopathy will have clinical deterioration with expectant management [11].

The initial workup for myelopathy begins with plain radiographs of the cervical spine. AP and lateral views typically demonstrate spondylotic changes including loss of disc height and uncinate and facet joint arthrosis. Radiographs allow evaluation for ossification of the posterior longitudinal ligament and assessment of lordotic versus kyphotic cervical spine alignment. Flexion and extension views should be obtained as dynamic instability and translation can contribute to cord compression. If myelopathy is suspected, MRI is critical for diagnosis as it allows visualization of soft tissues causing cervical stenosis and cord compression. In long-standing or severe myelopathy, MRI may demonstrate irregular changes within the spinal cord on T2 imaging known as myelomalacia. Myelomalacia represents cord edema and potentially irreversible necrosis and neuronal loss [12]. In cases where MRI is unavailable or contraindicated, CT myelogram may be used as a comparable alternative. If a patient has significant lower extremity symptoms such as gait ataxia, weakness, and pathologic reflexes but MRI of the cervical spine shows only mild or moderate stenosis, a thoracic spine MRI should be used to rule out a more caudal compression (Fig. 23.2).

There is little role for nonoperative management in the setting of cervical myelopathy [9]. Cervical stenosis without overt myelopathy can be treated with conservative therapy and close monitoring for symptom development. Additionally, those with very mild myelopathy choosing to avoid surgery or poor operative candidates may be followed closely clinically and radiographically given the fact myelopathy rarely progresses within the first 2–3 years of presentation [11]. Nonoperative treatment is similar to those of cervical radiculopathy. A combination of temporary immobilization, NSAIDs, acetaminophen, lifestyle modifications, and physical therapy can provide pain relief. It is crucial to counsel myelopathic patients on the increased risk of spinal cord injury with neck hyperextension. Counseling includes fall prevention and avoidance of situations potentially resulting in whiplash Hyperextension can result in spinal cord injury, commonly in the form of a central cord syndrome [13].

It is very difficult to determine which patients will develop neurologic decline. Majority of those diagnosed with cervical myelopathy require surgical intervention as 20–62% will have deterioration without surgery [9]. General indications for surgery include significant or progressive myelopathic symptoms, overt weakness, or gait disturbances [13]. Goals of surgery are to prevent further neurologic decline and reduce risk of spinal cord injury [9]. Operative intervention is very effective at preventing further decline but does not ensure recovery to baseline neurologic function. Majority will have improvement of gait and weakness, but postoperative improvement is variable. Surgical techniques are beyond the scope of this chapter. In general, the anterior approach to the cervical spine is again the workhorse for myelopathy. Anterior cervical decompression and fusion with or without corpectomy can be used for one- or two-level disease in either lordotic or kyphotic spinal alignment. Operative approach for multilevel disease at three or more levels is dependent upon spinal alignment. Posterior decompression

Fig. 23.2 Sagittal T2 MRI showing significant cervical stenosis most severe at C2–4 (left). Intraoperative fluoroscopy showing posterior cervical decompression and fusion (right)

and fusion should be used when there is 10 degrees or less of kyphotic alignment. In contrast, 13 degrees or more of fixed kyphotic alignment requires a combined approach with anterior and posterior decompression and fusion [6].

23.2 Lumbosacral Radiculopathy

Lumbosacral radiculopathy is a nonspecific clinical description of a disease process affecting lumbar or sacral nerve roots. Similar to cervical radiculopathy, lumbar radiculopathy is multifactorial. Spondylosis and degenerative disc disease results in nerve impingement. Etiologies include intervertebral disc herniation and hypertrophy of surrounding bony and soft tissues resulting in stenosis of the central spinal canal, lateral recesses, or neural foramen [14].

Lumbar radiculopathy presents with any combination of axial back pain, radiating leg and buttock pain, numbness, tingling, and paresthesias. Radicular pain is classically described as burning or sharp pain occurring in the dermatome of the affected nerve. Sitting, hip flexion, and knee extension typically worsen radicular pain [1]. Physical exam may elicit weakness and diminished reflexes of affected myotomes. Straight leg raise test places tension on affected nerves and indicates impingement if it reproduces radiating pain between 30 and 70 degrees of hip flexion.

When evaluating lumbar radiculopathy, it is important to assess for "red flag" symptoms. A history of malignancy, unintentional weight loss, severe nighttime pain, chills, fevers, and intravenous drug usage all warrant expedited evaluation. Progressive weakness and intractable pain are atypical and require investigation. Cauda equina syndrome is a true surgical emergency and requires surgical decompression. Acute low back and radicular leg pain with perineum anesthesia

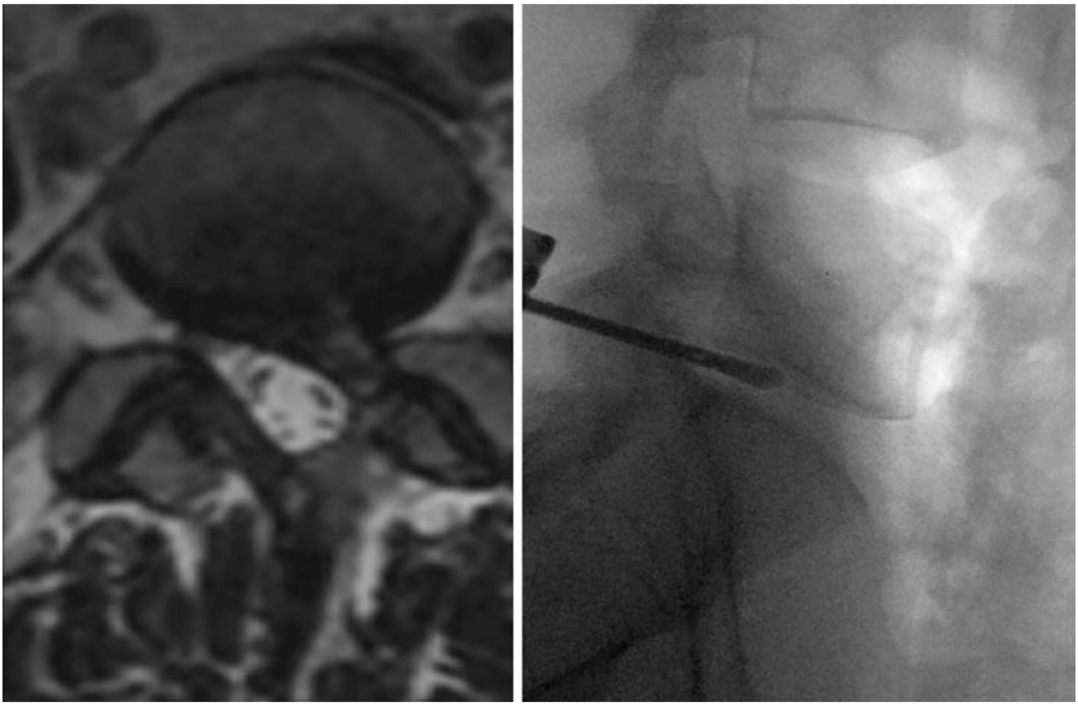

Fig. 23.3 MRI showing large left-sided posterolateral disc herniation at L5–S1 disc level compressing the traversing S1 nerve root (left). Intraoperative fluoroscopy showing a left L5–S1 microdiscectomy with decompression of the nerve root

("saddle anesthesia") bowel or bladder dysfunction should be treated as cauda equina and necessitate immediate imaging and diagnosis [15].

Diagnosis of lumbar radiculopathy (as with other forms of nonspecific low back pain) begins with a thorough history and physical exam. In the absence of "red flag" symptoms, diagnostic imaging can be deferred for 6 weeks as the majority of patients with radiculopathy will have spontaneous improvement [16]. Diagnostic imaging should be obtained if there is no significant improvement after 6 weeks. AP and lateral plain films of the lumbar spine are obtained first. While X-ray cannot show a herniated nucleus pulposus, it is used to evaluate for spinal alignment and concurrent pathologies (e.g., spondylolisthesis). MRI and CT myelography are equally sensitive for diagnosis of herniated nucleus pulposus [17]. In the absence of contraindications, MRI is the imaging study of choice as it allows better visualization of soft tissues, avoids ionizing radiation, and is less invasive compared to CT myelography (Fig. 23.3).

There is great difficulty defining the natural history of acute disc herniation and resultant lumbar radiculopathy as many patients will receive some form of treatment. Similar to cervical radiculopathy, lumbar radiculopathy is generally self-limited. Ninety percent of patients will have significant improvement with no treatment or nonoperative modalities at 6 weeks. Approximately 10% will have significant pain after 6 weeks and require workup and surgical intervention. Studies using sequential MRIs demonstrate decreased disc burden in 66% of patients after 6 months [16]. The landmark SPORT trial compared operative versus nonoperative treatment of lumbar radiculopathy with at least 6 weeks of persistent radicular pain. The SPORT trials found that both operative and nonoperative groups will have significant improvement of symptoms. However, those undergoing

surgical discectomy had a more rapid improvement of symptoms with reported improvement of physical function and overall satisfaction at 1 and 2 years postoperatively [18].

Treatment of lumbar radiculopathy begins with multimodal nonoperative interventions. Analgesics including NSAIDs and acetaminophen are the mainstay of pharmacologic management. A study by Rassmusen-Barr et al. found NSAIDs did not provide significant improvement in overall pain versus placebo, but NSAIDs did lead to better global functioning scores compared to placebo. Patients may benefit from a short steroid taper to decrease inflammation. This should be combined with activity modification and physical therapy, although the evidence supporting these interventions is lacking, likely secondary to the self-limited nature of radiculopathy. Activity modification is an important aspect of treatment; generally patients are able to self-identify activities and positions that minimize pain. It is important to state that activity modification does not imply complete bed rest. A systematic review by Hagen et al. found no benefit for complete bed rest in patients with acute low back and sciatica [19]. Once acute, severe symptoms resolve, physical therapy should be encouraged.

As discussed, prior, approximately 90% with lumbar radiculopathy will have improvement of symptoms with nonoperative treatment after 6 weeks. There is no evidence currently supporting early surgical intervention in the absence of severe or progressive neurologic deficits. The SPORT trials demonstrated patients will improve with and without surgical intervention after 6 weeks of persistent symptoms, but surgery will more rapidly relieve pain [18]. General indications for surgery include continued symptoms despite adequate period of nonoperative treatment and severe, progressive pain and weakness. The pattern of disc herniation dictates the surgical approach. Most commonly a herniated nucleus pulposus can be excised via midline laminotomy and discectomy ("microdiscectomy"). A paraspinal approach is utilized for a far lateral herniated discs causing foraminal stenosis.

23.3 Lumbar Stenosis and Neurogenic Claudication

Lumbar stenosis is defined as narrowing of the central or lateral recesses of the spinal canal secondary to impingement by surrounding bony architecture and soft tissues. This can result from degenerative and bulging intervertebral discs, ligamentum flavum hypertrophy, facet arthropathy, and facet cysts. Most commonly lumbar stenosis results from spondylosis and degenerative changes although there may be a component of congenital stenosis with short pedicles [20].

The most common symptom in lumbar stenosis is low back pain that progresses to involve the buttock and lower extremities. Classically, lumbar stenosis will present with neuroclaudication ("pseudoclaudication"). Neuroclaudication is a clinical diagnosis presenting as pain and heaviness of the lower extremities and associated weakness with prolonged standing, walking, and lumbar hyperextension which worsens stenosis. A study by Amundsen et al. found 91% of patients with lumbar stenosis have neuroclaudication [21]. Pain and heaviness associated with neuroclaudication will drastically improve with lumbar forward flexion but is not improved by standing still [22]. This is in contrast to vascular claudication that worsens with prolonged walking but improves when standing still and resting.

There is lacking data regarding the natural history of lumbar stenosis. In general, it is a slowly progressive disease process. A study by Johnsson et al. found 70% of patients with moderate spinal stenosis had no change in symptoms at 4-year follow-up. Fifteen percent had improvement of symptoms, while 15% had progressive worsening of symptoms [23]. The SPORT trials published in 2012 evaluated the outcomes over 4 years for lumbar stenosis treated with surgery versus nonoperative treatment. Participants in the study were required to have at least 12 weeks of persistent symptoms. At 4-year follow-up, those undergoing surgical laminectomy and decompression had significant improvement in pain, global function, and disability scores compared to the nonoperative treatment arm (using as-treated analysis). Sixty percent undergoing sur-

gery had at least a 15-point improvement on the Oswestry Disability Index compared to just 32% in the nonoperative group (p-value <0.001) [24].

Diagnosis of lumbar stenosis begins with plain radiography of the lumbar spine. This allows evaluation of spinal alignment, spondylotic changes including loss of disc height, and osteophyte formation. The spinal canal can be measured on lateral X-ray; stenosis is defined as a canal diameter of 13 mm or less. Flexion and extension X-rays can identify instability and spondylolisthesis which contributes to dynamic spinal stenosis (defined as >5 mm of vertebral translation or 10–15 degrees of vertebral rotation). MRI is used for evaluating central and lateral recess stenosis, allowing noninvasive imaging of the nerve roots and possible compression. Lumbar MRI is as equally sensitive as CT myelography for diagnosis of stenosis but is less invasive [22]. If there are atypical features of neuroclaudication or concern for vascular claudication, an ankle-brachial index is a simple and noninvasive evaluation for peripheral vascular disease.

Treatment for lumbar stenosis and neuroclaudication begins with nonoperative management. Initial options include NSAIDs, acetaminophen, exercise programs or physical therapy, and epidural steroids. Fifty percent of patients will have relief of pain and improvement of symptoms at 3 months with nonsurgical treatment [22]. Surgery is indicated for patients that do not improve with nonsurgical treatment and those with severe pain and intractable neurologic symptoms. Posterior lumbar laminectomy and decompression is the mainstay of surgical treatment for central and lateral recess stenosis. Laminectomy with fusion is indicated when there is severe foraminal stenosis (requiring extensive or complete facetectomy) or instability (secondary to concurrent spondylolisthesis [22].

23.4 Vertebral Compression Fractures: Osteoporotic Versus Malignancy-Associated Compression Fractures

Vertebral compression fractures are wedge-shaped fragility fractures of the spine due to compressive failure of the anterior vertebral body. Most commonly vertebral compression fractures are due to low bone mineral density in osteoporosis, although they can result from trauma, infection/osteomyelitis, and neoplasm. Thoracolumbar compression fractures occur following flexion-compression injury. In severe osteoporosis with poor bone quality, these fractures can occur from even trivial events such as lifting objects or riding in an automobile. Up to 30% of fractures may occur while the patient is in bed [3]. In patients without osteoporosis, compression fractures may occur in severe trauma. In patients younger than 55 years old presenting with a compression fracture following minimal trauma, malignancy must be ruled out.

Pain is the primary symptom in compression fractures. Pain is described as midline and localizes to the level of the fracture. Classically, vertebral compression fractures will have focal tenderness worse with percussion. Compression fractures rarely cause neurologic symptoms: radiating radicular pain and spinal cord compression is very rare. When there are numerous compression fractures with resultant kyphotic angulation of the spine, it may result in cord compression and neurologic compromise [8]. Warning signs for vertebral compression fractures include a history of malignancy, unintentional weight loss, severe nighttime pain, fever, chills, and intravenous drug usage. Additionally, neurologic deficits including lower extremity weakness and sensory deficits are atypical and require expedited workup and management.

The VERTOS II trial followed vertebral compression fractures treated nonsurgically to determine natural history. Sixty percent of patients had significant improvement of pain with nonoperative management; almost all had relief of pain within 3 months of diagnosis. In contrast, 40% had disabling pain that persisted 1 year after diagnosis. VERTOS II concluded that 3 months after diagnosis marks a cutoff for clinical decision making: if there is persistent, disabling pain after 3 months, then the patient is unlikely to spontaneously improve [25].

Diagnosis of vertebral compression fractures begins with AP and lateral plain radiographs. In the setting of significant trauma, X-rays of the full spine should be obtained to avoid missing

concurrent injuries. Upright X-rays of the spine are preferred as this allows measurement of the kyphotic angle and future comparison for progression of angulation [8]. In the setting of complex fracture patterns, CT is best to define bony anatomy. MRI and CT myelography are typically not necessary for vertebral compression fractures except in special cases. MRI is required to evaluate for cord compression if there are neurologic deficits or for identifying an underlying infectious or malignant process. Similarly, MRI can be used to gauge toe chronicity of a fracture and whether there is persistant intability or motion through the fracture. CT myelography is an invasive alternate form of advanced imaging if MRI is contraindicated and there remains concern for spinal cord compression.

Treatment for nonmalignant lesions begins with nonoperative management. The main goal of therapy is pain relief with early mobilization and avoidance of morbidity associated with prolonged bed rest. Symptomatic management is multimodal. Other issues related to acute low back pain are also discussed in Chap. 24. Analgesics include NSAIDs, acetaminophen, muscle relaxants, opiates, and neuropathic agents (gabapentin, SNRIs, TCA antidepressants, etc.) [26]. Despite severe, acute pain associated with compression fractures, physical therapy has proven efficacy. Malmaros et al. found patients participating in physical therapy had decreased pain and analgesic use, improved back extension strength, and improved quality of life [27]. Some patients may benefit from temporary bracing for 6 to 8 weeks after fractures, although the data supporting this is lacking [28]. Medical management must address the underlying osteoporosis to increase bone quality and decrease chance of additional fractures [29]. There is evidence showing calcitonin decreases pain and increases mobility in the first 4 weeks after injury [28]. Diagnosis and treatment of osteoporosis is beyond the scope of this chapter.

Despite multimodal pain management, up to 40% of patients have persistent pain after 12 months [25]. While there is no well-defined time frame for nonsurgical treatment, persistent symptoms for 3–12 months can be considered a failure of nonoperative treatment and vertebral augmentation procedures can be considered. The American Academy of Orthopaedic Surgeons (AAOS) guidelines from 2012 recommend against vertebroplasty since studies show minimal benefit compared to sham surgery. In contrast, the AAOS recommends kyphoplasty as an appropriate procedure for neurologically intact patients despite limited evidence [28]. Kyphoplasty is a percutaneous procedure that uses a balloon to restore vertebral height followed by cement injection. Contraindications for kyphoplasty include vertebra plana (complete collapse of vertebral body), bony retropulsion into the spinal canal, neurologic deficits, and active vertebral osteomyelitis. Open surgical decompression and fixation is required in the rare situations where compression fractures cause bony retropulsion or vertebra plana [29].

Management of malignant and infectious lesions of the spine (including compression fractures) is beyond the scope of this chapter. Advanced imaging with MRI or CT is required if there is concern for either. Workup will necessitate tissue biopsy of the lesion to guide further treatment.

23.5 Spondylolisthesis: Isthmic Versus Degenerative Spondylolisthesis

Spondylolisthesis is a condition where one vertebral body has translated or subluxated relative to an adjacent vertebra. There are five classifications of spondylolisthesis; the two most common are adult isthmic spondylolisthesis and degenerative spondylolisthesis [1]. Spondylolysis, which refers to a defect in the pars interarticularis (known to as the "isthmus"), is the driving force in adult isthmic spondylolisthesis. Spondylolysis, either a unilateral or bilateral pars defect, is common with a prevalence of 4–6% in the general population. Initial isthmic injury is believed to occur between ages 5 and 7 years. This can result from microtrauma and fatigue fracture, an elongated pars after healing of microtrauma, or acute traumatic fracture. Spondylolisthesis is very unlikely to occur with unilateral spondylolysis.

In contrast, bilateral pars defects will lead to symptomatic spondylolisthesis in approximately 40–66% [30]. Pars defects commonly occur in the L5 vertebrae allowing anterior slippage of the L5 vertebral body over S1. In contrast, degenerative spondylolisthesis does not have a pars defect and therefore has an intact neural arch, differentiating it from the isthmic form. Degenerative changes in the facet joints and intervertebral discs lead to intersegmental instability allowing vertebral slippage. Degenerative spondylolisthesis commonly affects the L4–L5 joint allowing anterior slippage of L4 on L5 [1]. Similar to other spinal pathology, the natural history of degenerative spondylolisthesis is not well characterized. Matsunga et al. followed degenerative spondylolisthesis in 40 patients for 5–14 years after initial diagnosis. Thirty percent of patients had radiographic progression of slippage, but none had clinical deterioration or worsening. Ten percent had clinical deterioration without radiographic progression. In general, the study found no correlation between radiographic progression and progression of symptoms [31].

There is significant overlap of symptomatology for these two forms of spondylolisthesis. The most common initial presentation of adult isthmic spondylolisthesis is nonspecific low back pain [19]. Over half of patients will have concurrent lower extremity pain which can be attributed to lumbar radiculopathy [32]. Neurogenic claudication is relatively uncommon because only the anterior elements of the vertebrae slip forward without an intact neural arch and therefore rarely cause central canal stenosis [10]. If there are radicular symptoms, it classically will affect the L5 nerve root in an L5–S1 spondylolisthesis. This results from foraminal stenosis secondary to hypertrophy of the pars lesion and L5–S1 disc bulging that compresses the exiting L5 nerve root [30]. Degenerative spondylolisthesis most commonly presents with low back pain. In contrast to isthmic, the degenerative form more commonly has symptoms of neurogenic claudication, similar to lumbar spinal stenosis. This is due to the intact neural arch of L4 translating anteriorly with the vertebral body and narrowing the spinal canal. Patients can have radicular leg pain due to L5 nerve root compression. When L4 slips anteriorly over L5, the inferior articular facet of L4 can cause lateral recess stenosis and subsequent impingement on the L5 traversing nerve root [1].

Diagnostic imaging begins with plain films of the lumbar spine and should include flexion and extension films allowing for evaluation of translational instability. Advanced imaging options include CT, SPECT CT, and MRI. CT of the lumbar spine allows visualization of the bony anatomy and pars defects if present. MRI further delineates soft tissues and is used for evaluating both central canal stenosis and neural foraminal stenosis [32]. In the setting of isthmic spondylolisthesis, SPECT CT may be used to distinguish acute pars defects from chronic defects [1] (Fig. 23.4).

Treatment for isthmic spondylolisthesis begins with initial nonoperative management. Activity restrictions include avoiding lumbar hyperextension. NSAIDs, acetaminophen, and physical therapy for core strength and flexibility are the mainstays of nonsurgical care. A trial of bracing and epidural injections may be used in acute pars fractures [1, 30]. Operative intervention is reserved for patients with incapacitating pain despite adequate trial of nonsurgical therapy for 6 months [10]. Additional indications include progressive or severe neurologic deficits, progressive slippage, and, very rarely, cauda equina syndrome [1]. Surgical fixation typically involves L5–S1 or L4–S1 posterior lumbar decompression and fusion depending on grade of listhesis. Anterior lumbar interbody fusions can be used in fusion constructs for low-grade spondylolisthesis.

Similarly, degenerative spondylolisthesis is initially managed nonoperatively. Nonsurgical therapy begins with NSAIDs, acetaminophen, physical therapy, and activity restriction. A trial of epidural steroid injections is appropriate if symptoms fail to improve. Surgical indications for degenerative spondylolisthesis include persistent, incapacitating pain that fails nonoperative treatment, worsening motor deficits, or cauda equina syndrome [1]. Most commonly, a posterior lumbar decompression and fusion is indicated. Alternatively, laminectomy with anterior

Fig. 23.4 Sagittal T2 MRI demonstrating lumbar stenosis at L4–L5 with anterolisthesis of L4 secondary to degenerative spondylolisthesis (left). Postoperative lateral XR demonstrating sequelae of L4–L5 posterior lumbar decompression and fusion

lumbar interbody fusion may be used. The SPORT trials followed patients with degenerative spondylolisthesis and symptomatic spinal stenosis for 4 years. The study found that patients treated surgically had greater improvement of pain, function, and disability scores and higher self-rated progress at 4 years compared to patients treated nonsurgically. Using as-treated analysis, the SPORT trial found that the surgical cohort had an absolute improvement of 33% of back pain scores and 55% improvement of leg pain scores compared to the nonoperative cohort [33].

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24 Low Back Pain

Lincoln Pratson and Daniel Cavanaugh

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the key concepts, principles of diagnosis, and common clinical findings of patients with low back pain
- *Objectives*: On completion of this unit, the reader should be able to define and describe these aspects of low back pain:
  1. Epidemiology
  2. Differential diagnosis of low back pain
  3. "Red flag" conditions that should warrant particular care on the part of the clinician
  4. Physical examination and approach to imaging for these patients
  5. Principles of nonsurgical management
  6. Principles of surgical management

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24.1 Definition and Epidemiology

Low back pain is a common clinical condition with most people experiencing low back pain during at least one point in their life [1] and represents the fifth most common reason for visits to physicians [2]. In a global study, low back pain was the highest cause of disability and the sixth most common medical condition cause of overall burden [3]. Low back pain also represents a significant financial burden on the healthcare system and society with the total annual costs associated with low back pain in the United States exceeding $100 billion. Direct healthcare costs of treating low back pain are estimated to be roughly $86 billion in 2005, and 2% of the US workforce are compensated for low back pain in a given year. Given the prevalence of low back pain and associated morbidity, it is imperative for orthopedic practitioners to be familiar with the common and less common, but more serious, causes of low back pain. This chapter will discuss how to properly evaluate, diagnose, and treat both specified and unspecified low back pain.

Many patients with low back pain experience self-limited episodes of pain. Most of those who seek care will experience improvement in pain, disability, and ability to return to work within the first month [4, 5]. However, up to one third of patients will have persistent symptoms after 1 year, with one in five patients reporting substantial limitations in activity [1, 6].

24.2 Evaluation of Low Back Pain

While a standardized assessment of low back pain does not exist, a practical approach developed by the American College of Physicians and the American Pain Society in the Joint Clinical Practice Guideline Diagnosis and Treatment of Low Back Pain [7, 8] recommends performing a focused history and physical examination that aims to classify patients into one of three broad categories: non-specific low back pain, back pain associated with radiculopathy or spinal stenosis, and back pain associated with another specific spinal cause. This helps guide decision-making as well as identifies the less common but more serious conditions that require prompt evaluation. The American College of Physicians and the American Pain Society have developed a standardized approach to the evaluation and management to low back pain in the Joint Clinical Practice Guideline Diagnosis and Treatment of Low Back Pain [7, 8].

Proper diagnosis demands a thorough history as part of the initial evaluation, beginning with symptom chronicity. It is imperative to delineate between acute and chronic back pain as most episodes of acute back pain are self-limiting and require only symptomatic treatment. In contrast, chronic or worsening back pain can indicate the need for a more in-depth work-up. A thorough review of the type of pain experienced should include the *character* (e.g., somatic pain (aching and well-localized) vs. neuropathic pain (stabbing, shooting, or burning)), the *location* (e.g., axial vs. appendicular as well as laterality), *associated factors* (e.g., numbness, paresthesias, weakness), and *modifying factors* (e.g., alleviating and aggravating factors).

Evaluation for r*ed flag* signs should be included as part of any initial assessment of low back pain. These refer to commonly identified symptoms that are often used to help identify pathology that requires a more urgent work-up. It is important to note that these signs by themselves do not rule in or out certain conditions and should be used in conjunction with the rest of the history and exam as a number of studies have shown that when used in isolation, they can result in a significant number of false positives. These “red flag signs” include:

- Bowel or bladder dysfunction (most commonly urinary retention)
- Progressive neurologic weakness
- Perianal or “saddle” anesthesia
- Bilateral radiculopathy
- Unrelenting night pain

It is important to obtain a good general medical history during initial evaluation of low back pain in order to further rule out the less common but more serious etiologies of low back pain. These include:

Cancer: The spine is the third most common site of cancer metastasis [7] with metastasis accounting for 97% of cancers involving the spine [8]. The most common tumors that metastasize to the spine originate from the breast, prostate, kidneys, thyroid, and lungs [9]. In addition, hematologic malignancies such as multiple myeloma and lymphoma can also affect the spine (Fig. 24.1). Spinal tumors must be differentiated from infection. Typically, spinal metastasis will spread hematogenously and therefore spread to vascular dependent areas, namely, the vertebrae, whereas infection will more commonly involve avascular areas like the vertebral disc. A prior or current history of cancer significantly increases the likelihood of spinal malignancy [10, 11]. Other suggestive signs cited in some guidelines include older age, weight loss, and failure to improve after 1 month of low back pain. These factors had high false-positive rates in isolation and therefore are most useful when combined with a history of cancer [11].

Fig. 24.1 T2-weighted MRI of a 63-year-old man with diffuse large B-cell lymphoma. Note the abnormal signal in the L3 vertebral body and associated mild compression fracture

Infection Infection of the spine is a less-common but important pathology that must be recognized promptly. Despite the fact that spinal infection can often present with identifying factors, such as fever, elevated inflammatory markers (CRP, ESR), or suggestive history (IV drug use), it is commonly missed [12]. Acute spinal infections are most often pyogenic and can be seeded from any source of infection with UTI being the most common cause. Chronic infections may be pyogenic, fungal, or granulomatous, and therefore a wide variety of etiologies such as tuberculosis should be ruled out. Strong predictors of infection include severe pain, a history of lumbar surgery within the past year, the presence of a fever, a urinary tract infection, or wound that communicates in close proximity to the spine. Weaker signs include a history of IV drug use, pain increased or unrelieved by rest, vertebral tenderness, and limited spin range of motion.

Cauda equina/spinal cord compression Cauda equina refers to compression with loss of function of two or more of the 18 nerve roots that make up the lumbosacral spinal cord and nerve roots. It most often occurs secondary to a disc herniation or space-occupying lesion but can also be due to infections (meningitis), complications from surgery, anesthetic procedures, spinal manipulation or epidural injections. While presenting symptoms vary, loss of sensation and bladder involvement are the most common, followed by fecal incontinence and perianal numbness or “saddle anesthesia” [13]. Although spinal cord compression is rare (present in <0.04% of patients with severe low back pain) [14], all evaluations of new or worsening low back pain should include evaluations for these red flag symptoms.

Vertebral compression fracture: Between 1% and 4% of patients presenting with complaint of low back pain have a fracture which is important to identify for preventing contraindicated therapies such as manual manipulation as well as identifying the need for further work-up of potential causes as osteoporosis [15]. Suspicion for vertebral compression fracture should be higher with a suggestive mechanism (a fall from a height or motor vehicle crash in a young patient), a history of osteoporosis (especially when presenting with a mechanism of a minor fall or heavy lifting), age (men >65 and females >75), a prolonged use of corticosteroids, focal tenderness, and/or the presence of contusion or abrasion [16, 17]. The likelihood of a fracture increases significantly with any combination of these presenting details [10].

A psychosocial assessment should also be included in evaluations of low back pain as psychiatric illness, especially depression, is common in chronic low back pain and has been shown to influence reported pain levels.

Physical examination of low back pain should include visual inspection, noting any obvious deformity (scoliosis), scars, rashes, swelling, as well as an evaluation of the patient's gait. Palpation should be performed, noting for any tenderness and the location if present. The patient should be ranged through lumbar flexion, extension, lateral bending, and rotation. A good neurologic exam should be performed, including dermatomal sensation, strength, reflex testing, and upper motor neuron signs including Babinski and clonus evaluation. Certain special tests should be included as part of a physical exam for low back pain. These include the Straight Leg Raise test in which the patient is in supine position and the patient's affected or unaffected leg is lifted by the heel, keeping the knee extended. This test has been shown to be 90% sensitive and 25% specific on the affected side but 30% sensitive and 90% specific on the unaffected side [18]. The Reverse Straight Leg Raise test involves the patient in the lateral position with the affected extremity toward the ceiling while the examiner extends the hip and flexes the knee. Provocation of radicular symptoms can be positive with existing L3–L4 pathology. The sacroiliac (SI) joint is a common source for low back pain, and there are four common provocative exam maneuvers that can be used to rule in or rule out SI pathology: distraction, thigh thrust, compression, and sacral thrust. When two or more of these four maneuvers are able to reproduce the patient's symptoms, the patient will likely benefit from a SI joint injection. When all four of the maneuvers fail to reproduce the patient's symptoms, the SI joint is highly unlikely to be the pain generator in the patient [19]. A hip exam including range of motion, strength evaluation, and special tests such as log roll and Stinchfield should be completed to evaluate for pathology that can overlap in pain presentation with low back pain such as hip osteoarthritis.

24.3 Imaging

Lumbar imaging as part of the initial evaluation of patients with non-specific or radicular low back pain with an absence of red flags on clinical presentation is not recommended. A 2009 meta-analysis with over 1800 patients with acute low back pain and no clinical or historical features that suggested a specific underlying condition found no differences between patients treated with routine lumbar imaging (radiography, MRI, or CT) and those treated with usual care without routine imaging in terms of pain, function, quality of life, or overall patient-rated improvement [20]. Imaging is indicated in certain patients, including elderly patients and patients with low-velocity trauma; patients with osteoporosis and chronic steroid use; patients in whom there is a suspicion of cancer, infection, or immunosuppression; patients who are surgical or intervention candidates with persistent or progressive symptoms during or following 6 weeks of conservative management; patients with new or progressive symptoms or clinical findings with history of prior lumbar surgery; and patients with low back pain with suspected cauda equina syndrome or rapidly progressive neurologic deficit [17].

When imaging is indicated, lumbar radiography is the initial imaging of choice with AP and lateral views typically obtained. Lumbar radiographs can adequately demonstrate fractures as well as degenerative disc disease. In situations where radiographs are indeterminate, CT is the next suggested modality [21]. Computed tomography (CT) scans provide a more in-depth and 3D evaluation of bony architecture for conditions such as degenerative changes, fractures, and fusion as compared to radiographic imaging. CT has replaced radiography as the modality of choice for patients with known trauma to the spine for evaluation of fracture, dislocation, or subluxation [20]. It is also useful for preoperative planning for evaluation of pedicle screw morphology and sizing. CT, however, is not ideal for visualizing soft tissues. CT with contrast (including CT myelography) can be used for better visualization of infectious processes and tumors in patients for whom MRI is contraindicated (e.g., pacemaker implant). CT contrast can demonstrate rim enhancement of fluid collections, increasing suspicion for infectious processes as well as heterogeneity of soft-tissue tumors. CT carries significant radiation exposure with a single spine CT scan corresponding to the natural radiation one receives over 2 years. MRI is the third commonly used imaging modality in the spine. It is better in evaluating soft-tissue structures (paraspinal soft tissues, intervertebral discs, spinal cord, and nerves) than CT and radiographs and does not pose the risks associated with radiation. The two most commonly used MRI sequences in evaluating the spine are T1- and T2-weighted sequences. The T1-weighted sequences (fat as hyper-intense and water as hypo-intense) are primarily used to evaluate bone edema. If marrow appears darker than the paraspinal muscles, then a pathologic process should be considered. T2-weighted sequences (water and fat are both hyper-intense) are better suited for evaluation of spinal cord and nerve compression as well as disc pathology (annular tears, disc protrusions/extrusions). Bone scintigraphy and PET are modalities most often used in the identification and diagnosis of spine disease, fractures, osteomyelitis, and osteolytic metastatic tumors all of which show increased ("hot") activity in a bone scan. PET scanning is most commonly used for the detection of spinal metastasis as it can identify both bone and soft-tissue tumors [22]; however it is important to note that any process with increased glycolytic activity (infection, inflammation, etc.) can lead to false positives as PET imaging.

As with all diagnostic modalities, imaging findings should be interpreted in the clinical context of the patient. Multiple studies have demonstrated the significant number of asymptomatic subjects with identified degenerative disc pathology [23, 24].

24.4 Common Causes of Low Back Pain

24.4.1 Non-specific Low Back Pain

In 85% of patients, the cause of the low back pain cannot be reliably attributed to a specific disease or structural spinal abnormality [25]. Several etiologies for non-specific low back pain have been postulated, the two most common of which have been *discogenic* and *facetogenic*.

Discogenic pain refers to the intervertebral disc as the pain generator for low back pain. The intervertebral disc is made up of three components: the central nucleus pulposus, the surrounding annulus fibrosus, and the vertebral end plates of the vertebral body superior and inferior to the disc. The nucleus pulposus is the gelatinous center of the disk and is composed primarily of water and large proteoglycans that are held in place by the surrounding annulus fibrosus. As the intervertebral disc ages, the disc dehydrates and collapses in height secondary to loss of water within the nucleus pulposus causing the surrounding annulus to protrude out. The most common direction of protrusion is posteriorly in the lumbar spine. Studies have demonstrated the presence of nociceptive nerve fibers in the posterior longitudinal ligaments and in the outer layers of the annulus fibrosus, which are stimulated by pressure increased by loss of disc height and disc bulge. These stimuli likely combine with inflammatory

cytokines and mediators within the disc (prostaglandin E2, interleukin (IL)-6 and IL-8, TNF-alpha) that increase discogenic pain by irritating the nociceptive nerves and lowering the threshold for stimulation [26]. In a study of 170 patients with low back pain, disc degeneration was found to be the most common cause of low back pain (41.8%) and was shown to be associated with younger adults and males [27]. One of the identifying factors of discogenic pain is that it is worsened by lumbar flexion which leads to increased pressure within the intervertebral disc anteriorly, causing the disc to "pinch" out posteriorly. *Facetogenic* pain refers to the lumbar facet or zygapophysial joint as a pain generator for low back pain. The lumbar facet joints are true synovial joints that form the posterolateral articulation, which connects one vertebra to the adjacent vertebra. Similar to the intervertebral disc, there are a number of nociceptive neurons, including the medial dorsal rami surrounding the facet joint that fire when stimulated by stretch or pressure, and associated inflammatory prostaglandins and cytokines that likely increase the pain [28–31]. Both selective stimulation and anesthetic blocks of the lumbar facet joints have demonstrated respective reproducibility and reduction of low back pain in a significant number of patients [27, 32, 33]. Interestingly, while a number of basic science studies have demonstrated a relationship between the presence of degenerative disc disease and facet joint arthropathy [34, 35], they appear to be independent causes of low back pain [36]. A number of studies have attempted to locate specific referral patterns associated with the individual facet joints which could, in turn, guide treatment. However, there is wide overlap and discordance in the reported facet joint pain referral patterns. Upper lumbar facet joint pain tends to extend into the flank, hip, and upper lateral thigh, whereas pain from the lower lumbar facet joints usually penetrates lower in the thigh, usually laterally and/or posteriorly. All of the lumbar facet joints are capable of producing pain that can be referred into the groin [37]. Low back extension increases low back pain in facetogenic pain secondary to increases in the forces along the lumbar facet joints, in contrast to discogenic pain that increases with lumbar flexion.

Sacroiliac pain: The sacroiliac joint is estimated to cause 10–30% of chronic low back pain [27, 38]. Similar to low back pain in general, the etiology behind SI joint dysfunction and low back pain is often unclear. Some known causes of SI joint pain include remote pelvic ring fractures and pelvo-lumbar mismatch [38]. Sacroiliitis can also be a less common cause of low back pain and often presents opposite of typical low back pain in that it involves younger patients, is worse in the morning, and improves with activity. It is also often associated with inflammatory bowel diseases and HLA-B27. SI joint pain can be felt as pain radiating anteriorly into the thigh and even the groin. This necessitates a thorough hip examination when evaluating low back pain in order to rule out other causes of mimicking pain. Given the overlap of other causes of low back, hip, and groin pain as well as that SI joints are often radiographically normal in symptomatic patients, intra-articular anesthetic injections can be used to diagnose SI joint pain.

Spondylolisthesis: Spondylolisthesis refers to the translocation or "slip" of the superior vertebrae relative to the inferior vertebrae. This condition is discussed in Chap. 23.

Scoliosis: is a three-dimensional deformity of the spine with a coronal deformity greater than ten degrees and associated deformity in sagittal and axial planes (Fig. 24.2). Scoliosis can be further categorized into congenital and degenerative forms. Adolescent idiopathic scoliosis (AIS) is the most common cause of scoliosis. The cause of AIS is still unknown, but a familial component is suggested by increased prevalence in future generations with variable penetrance. AIS typically presents during adolescence and is commonly identified by truncal asymmetry [39]. While typically asymptomatic, AIS has been shown to be associated with a higher prevalence of musculoskeletal back pain [40]. Degenerative scoliosis refers to scoliosis in the skeletally mature individual. This includes further progression of AIS or de novo development of scoliosis. De novo degenerative scoliosis develops during adulthood due to the degeneration of spinal

Fig. 24.2 Anteroposterior radiograph of a 23-year-old patient with idiopathic scoliosis of the thoracolumbar spine

motion segments, primarily limited to the lumbar spine and generally beginning with the intervertebral disc deteriorating followed by the lack of integrity of the posterior components particularly the facet joints [41]. Adults typically present with symptoms of progressive back pain in addition to neurogenic claudication or spinal stenosis. However, forward flexion at the hip does not consistently relieve symptoms in patients with degenerative scoliosis as it does in typical spinal stenosis.

Lumbar disk herniations and spinal stenosis are discussed in Chap. 23.

24.4.2 Nonoperative Management

While a definitive treatment algorithm for newly presenting low back pain, a number of studies have provided varying evidence for the available treatment options, which can help guide initial management.

Medications: Nonsteroidal anti-inflammatory (NSAID) drugs are widely used for low back pain and have strong evidence demonstrating short-term symptomatic relief in patients with acute and chronic low back pain. However, no single NSAID has been shown to be more effective than any other in its class, and they are not without side effects. Acetaminophen has been demonstrated to be equally as effective as NSAIDs without a demonstrated additive effect [42]. Moderate-quality evidence exists for the use of muscle relaxants in the treatment of low back pain, particularly in the first 1 to 2 weeks from onset and that the effect can be additive when used in combination with NSAIDs [43]. Opioids are commonly prescribed for severe pain; however multiple studies have shown no difference in pain relief or time to return to work between oral opioids and NSAIDs or acetaminophen [44, 45] which is an important consideration given the significant comorbidities and addictive potential associated with opiate medications. Oral steroids have no demonstrated benefit in isolated acute low back pain but may be beneficial in treating radicular leg pain [46].

Patient education: Patient education and reassurance that low back pain is often benign and self-limiting has been shown to be effective in managing chronic low back pain [47]. Patient education should include recommendations to stay as active as possible within the confines of their symptoms and to avoid biomechanics that could worsen symptoms including twisting and bending especially when lifting [48].

Physical therapy: Moderate evidence exists for physical therapy-directed home exercise programs reducing the rate of recurrence and healthcare services as well as increasing the time

between back pain episodes [45, 49]. The McKenzie method is a physical therapy method for the management of low back pain that has been shown to be more effective than other back pain treatments, though not statistically significantly [50, 51].

Ice and heat: Ice and heat have been shown to have analgesic effects in the treatment of low back pain. Heat has been shown to be efficacious in the short-term period in the treatment of low back pain. There is a lack of evidence for the efficacy of ice in the treatment of low back pain [52]. However, unlike a number of the other treatments of low back pain, ice and heat application have minimal side effects when applied properly.

Acupuncture: There is limited evidence supporting acupuncture as a treatment of low back pain. However, it may be an effective adjunct to more traditional treatments for chronic low back pain [53, 54]. A recent meta-analysis demonstrated that acupuncture clinically reduces chronic low back pain and improves function, equal to or slightly greater than medications, though the strength of the available studies was limited [55]. Several level one studies demonstrated acupuncture as being significantly better than traditional treatment of physical therapy and medications, though there was no difference noted between actual and sham acupuncture in the treatment of chronic low back pain [47, 56].

Exercise: There is poor to moderate evidence supporting exercise (aerobic conditioning, strengthening, and/or flexibility exercises) as a treatment for low back pain; however it has been demonstrated to be at least slightly effective at decreasing pain and improving function in both acute and chronic low back pain [57].

Lumbar supports (e.g., bracing): Lumbar bracing has not been shown to be effective at preventing low back pain and conflicting evidence exists for its effectiveness in treating low back pain [58].

Spinal manipulation, chiropractic treatment, massage: Spinal manipulation may be effective in the short-term reduction of acute low back pain (1 month vs. 6 months); however there is no evidence that chiropractic techniques (including spinal manipulation) provide clinically relevant improvement in pain or disability as compared with other treatments [59]. Massage for chronic low back pain also lacks high-quality evidence; however it has been shown to relieve acute low back pain and for pain and function for chronic low back pain in the short term [60].

Yoga: Yoga is an increasingly popular practice in the United States with low back pain representing a significant reason for practicing yoga (~20%). In chronic low back pain patients, yoga has been shown to improve pain as well as increase flexibility, balance, and depression [61, 62].

24.5 Injections

As part of a comprehensive care plan, spinal injections can improve pain, allow for increased tolerance and participation in nonoperative interventions, reduce the need for surgery, and predict surgical outcomes. As discussed above, inflammatory mediators and neural nociceptive stimulation play a primary role in common causes of low back pain. Therefore, spinal injections delivering corticosteroid (an anti-inflammatory) and local anesthetics (which blocks nociceptive stimulation) understandably decrease low back pain. Diagnostic procedural injections are useful in confirming a source of pain when used in conjunction with a thorough clinical evaluation. Care must be taken when interpreting the diagnostic accuracy of injections however, as they have been found to produce a high percentage of false-positive results [63]. Lumbar steroid injection can be delivered several ways. *Caudal epidural steroid injections* are the least specific injections and occur through the sacral hiatus, filling the epidural space cephalad up to the level of L4–L5. Caudal epidural steroid injections are best for patients with suspected L5/S1 or L4/L5 pathology and in whom interlaminar or transforaminal steroid injections have been unsuccessful or are

unlikely to be successful (e.g., degenerative disc disease with severe joint narrowing, previous fusion surgery, severe scoliosis, etc.). *Interlaminar injections* can be performed between the levels of C6–C7 to L5–S1, typically through the paramedian approach. These injections are typically indicated for patients with bilateral symptoms such as spinal stenosis as the injectant will affect bilateral nerve roots as well as likely travel several levels cephalad and caudal [64]. This approach is contraindicated in patients with previous spinal fusion at the targeted level or with severe stenosis and inadequate posterior epidural space. *Transforaminal epidural injections* are the most specific of the three and can occur at any level. These injections are indicated for the relief of radicular pain. Any lumbar injection should occur under imaging as without imaging guidance, at least 30–50% of interlaminar and caudal epidural injections are incorrectly delivered. Transforaminal epidural injections also carry the highest risk for incorrect injection placement into a radicular artery.

Radiofrequency neurotomy (RFN): consists of imaging-guided thermal coagulation/ablation of a nociceptive-generating nerve, typically the medial branch of the innervating dorsal rami of the spinal facet joint. It has been shown to be effective in providing relief for facetogenic pain; however outcomes are highly dependent on technique and patient selection utilizing diagnostic blocks prior to proceeding with RFN [65].

24.6 Operative Management of Low Back Pain

General indications for surgery for low back pain include cauda equina symptoms, progressive motor deficit, motor deficit failing to show continued recovery at 1–3 months, and persistent pain lasting greater than 6 weeks despite conservative management. Surgery is not typically indicated in non-specific low back pain, as the results from surgery are unpredictable with over half of patients who undergo surgery for low back pain demonstrating no to minimal improvement in symptoms. In fact, patients that underwent spinal surgery for non-specific low back pain did no better than those who were treated nonoperatively by physical therapy with cognitive interventions. Some other aspects of operative treatment are discussed in Chap. 23.

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Common Clinical Conditions of the Shoulder

25

Robert J. Esther and Colleen B. Balkam

Contents

Goals and Objectives

- *Goal*: To introduce the reader to the common injuries to the shoulder girdle
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Incidence and relative frequency of common shoulder girdle injuries

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2. Basic presentation and examination of common shoulder injuries
3. Necessary imaging of particular shoulder injuries
4. Basic treatment principles of the common shoulder injuries

Fig. 25.1 Bilateral clavicle fractures. AP radiograph of a patient with bilateral middle third clavicle fractures. The right demonstrates minimal displacement, while the left side demonstrates greater than 100% displacement, significant shortening, and minimal comminution

25.1 Clavicle Fractures

Clavicle fractures account for 3–4% of all fractures, up to 10% of fractures of the upper extremity, and 44–66% of fractures about the shoulder. Middle third fractures are the most common and account for 80–85% of clavicle fractures. Lateral third fractures account for 15–20% and medial third approximately 5%. Clavicle fractures are classified by location and categorized into medial, middle, or distal third fractures. Treatment may be operative or nonoperative based on severity of the fracture [1].

The majority of clavicle fractures occur via axial loading after a fall or impact to the affected shoulder. More rarely these fractures may be caused by a direct blue, secondary to muscle contraction during a seizure, or minimal trauma through pathologic bone in the setting of infection or tumor.

Patients with clavicle fractures will present with splinting and refusal to move the affected arm. It is important to perform a complete neurologic exam as well as auscultation of the lungs. In rare instances, the brachial plexus, subclavian and axillary vessels, and superior lung – which are normally protected behind the middle third of the clavicle – may be injured as well. The proximal fragment is pulled superiorly by the pull of the trapezius and sternocleidomastoid (see Fig. 25.1). This displacement, when severe, may lead to skin tenting and necrosis [1].

The majority of clavicle fractures can be successfully treated nonoperatively with temporary immobilization in a sling or figure-of-eight brace for 4–6 weeks. The goal of immobilization is to provide comfort while allowing use of the ipsilateral hand and elbow. Active range of motion of the wrist and elbow is encouraged to prevent stiffness. Some degree of shortening and persistent angulation usually results from successful nonoperative management [3].

Indications for surgical fixation include greater than 2 cm of shortening on radiographs, superior displacement of one fragment greater than 100% of the width of the bone, and significant comminution as these factors significantly increase the risk of fracture nonunion. It is important to obtain radiographs with the patient in an upright position, as supine radiographs minimize the effect of gravity and may mask significant displacement. Other indications include open fractures or instances of skin tenting at risk for becoming open fractures, fractures with underlying neurovascular injury, or a floating shoulder injury in which a clavicle fracture is associated with a scapular neck fracture such that the arm is no longer in boney contact with the axial skeleton [3].

Surgical fixation may be achieved via open reduction and internal fixation with a plate and screw construct or intramedullary pinning. Precontoured plates allow stable fixation while minimizing hardware prominence. Postoperatively a small number of patients will report anterior chest numbness due to injury to branches of the suprascapular nerve, as well as prominent hardware.

The majority of clavicle fractures go on to heal with satisfactory outcomes. Complications include neurovascular compromise due to initial injury, iatrogenic injury during surgical fixation,

or compression by fracture callus or persistent deformity [1]. Malunion may cause a persistent bony prominence that patients may find cosmetically bothersome, as well as shortening that leads to decreased functional capacity of the arm. Nonunion is rare (between 0.1% and 13%), with the vast majority occurring in the middle third. Nonunion is associated with severity of initial trauma and open fracture, extent of displacement, soft tissue interposition, refracture, and inadequate period of immobilization [3].

25.2 Shoulder Separation: AC Joint Injuries

Acromioclavicular joint injuries and dislocations account for 9–10% of acute injuries about the shoulder. These injuries are significantly more common in males and are most common in the second decade of life. Athletes participating in contact sports or high-speed activities including cycling and skiing are at the highest risk [2]. These injuries are classified by degree of damage to the acromioclavicular and coracoclavicular ligaments and amount and direction of displacement of the clavicle. Treatment may be operative or nonoperative, based on the injury itself as well as patient activity level (Miller). These injuries may be associated with fractures of the clavicle, acromion process, or coracoid process.

The AC joint is a diarthrodial joint with minimal mobility through a meniscoid disk. The joint is stabilized horizontally by the AC ligaments (anterior, superior, posterior, and inferior) as well as fibers of the deltoid and trapezius muscles. Vertical stability is provided by coracoclavicular ligaments – the conoid which is medial and the trapezoid which is lateral. The average distance between the coracoid and the clavicle is 1.1–1.3 cm, which is used in classifying injuries to this joint [1].

Injuries to the AC joint typically occur via direct force to the superior and lateral shoulder with the arm in an adducted position, thus forcing the acromion inferiorly and medially versus a stable clavicle. Less commonly these injuries are caused by a fall onto outstretched arm with force directed through the humeral head forcing the acromion superiorly. The AC ligament is first to fail, followed by the CC ligaments in more severe injuries [2].

Patients will present with pain in the lateral shoulder. There may be an obvious droop of the affected shoulder or a palpable step-off of the joint with possible tenting of the skin by the displaced clavicle. Radiographs should be taken and patients examined while upright to stress the AC joint and accentuate deformity. In the case of questionable injury, radiographs of the contralateral side may be compared, or stress radiographs may be performed with the patient holding 10–15 pounds of weight in the affected arm [1].

AC joint injuries are classified based on the degree and direction of displacement of the distal clavicle (see Table 25.1). Type I injuries are characterized by AC ligament sprains with intact CC ligaments and normal radiographic appearance. Type II injuries have disrupted AC ligaments and sprained CC ligaments. The AC joint appears widened with less than 25% increase in radiographic CC distance. Type III injuries are characterized by disrupted AC and CC ligaments with 25–100% increase in the radiographic CC distance compared to the contralateral side and widening of the AC joint. Type IV injuries demonstrate disrupted AC and CC ligaments, increased CC distance, and posterior displacement of the clavicle. The joint cannot be reduced in a closed manner. Type V injuries have disrupted AC and CC ligaments, with 100–300% increase in CC distance, and typically demonstrate tenting of the skin by the distal clavicle. Type VI injuries are unique in that the clavicle is displaced inferiorly to the acromion with a decrease in CC distance. This injury is typically the result of high-energy trauma and commonly associated with clavicle and rib fractures and brachial plexus injury [1, 2].

Type I and II injuries can be managed nonoperatively with sling immobilization for 1 week for type I injuries and 1–3 weeks for type II injuries as well as NSAIDs, ice, and activity modification. When pain has resolved, patients begin physical therapy to regain range of motion and strength, but should remain out-of-contact sports

Table 25.1 Classification of AC joint separation

Type	AC ligaments	CC ligaments	Increase in CC distance	AC appearance	Clinical exam
I	Sprained	Intact	Normal (1.1–1.3 cm)	Normal	Point tenderness, minimal pain w/motion
II	Disrupted	Sprained	<25%	Widened	Distal clavicle displaced slightly superior
III	Disrupted	Disrupted	25–100%	Widened	Depression of the arm, skin tenting by the distal clavicle
IV	Disrupted	Disrupted	Increased	Posterior clavicle displacement	Distal clavicle is displaced posteriorly
V	Disrupted	Disrupted	100–300%	NA	Severe skin tenting by distal clavicle
VI	Disrupted	Disrupted	Decreased	NA	Flattened shoulder with prominent acromion. Associated with rib and clavicle fractures and brachial plexus fractures

until full restoration of painless range of motion. Management of type III injuries is controversial and must be decided on a case-by-case basis. Older patients with lower activity levels will likely do well with nonoperative management, while younger, more high demand patients may benefit from surgery. Type IV, V, and VI injuries should be treated with surgical reconstruction to prevent persistent shoulder pain, deformity, and dysfunction [2].

25.3 Shoulder Dislocations

The shoulder is the most commonly dislocated major joint with an incidence of 17/100,000 people per year. The distribution is bimodal with peaks in men between ages 20% and 30 and women between ages 61 and 80. 96% of dislocations are anterior, while the remaining 4% are posterior, and inferior and superior dislocations are exceedingly rare. After a single dislocation event, the incidence of recurrence is approximately 50% and even higher for patients who were younger at the time of initial injury [1, 2].

The glenohumeral joint moves through a large range of motion in many directions and is relatively shallow and depends on soft tissue attachments for the majority of stability. Static restraint is provided by the glenoid labrum, which functionally deepens the glenoid socket. The joint capsule provides limited stability due to inherent redundancy [2]. The inferior, superior, and middle glenohumeral ligaments are the primary restraints to anterior translation of the humeral head. The rotator cuff, long head of the biceps, and scapular stabilizing muscles provide dynamic support to the shoulder [1].

Dislocation of the joint involves a stretching or tearing of the joint capsule and may involve damage to the labrum. A Bankart lesion describes an avulsion of the anterior labrum off the glenoid rim, while a bony Bankart also involves a fracture of the glenoid rim. A Hill-Sachs lesion involves an impression fracture of the humeral head due to impact with the glenoid rim and is common anterior shoulder dislocations. Rotator cuff tears are also commonly associated with shoulder dislocations and should be suspected particularly in older patients or patients who are unable to lift their arm after reduction [1, 2].

Although the clinical exam is often sufficient for the diagnosis of a glenohumeral dislocation, radiographs should be obtained in first-time dislocators, older patients. Radiographs of a shoulder with concern for dislocation must include orthogonal views including an AP and axillary or Velpeau view (see Figs. 25.2 and 25.3). CT may be used to diagnose bony injury including Hill-Sachs or bony Bankart, while MRI is better for the assessment of soft tissues and can both be obtained after reduction if indicated.

25.3.1 Anterior Dislocation

Anterior dislocations account for 96% of shoulder dislocations and may result from direct in which an anterior directed force is applied to the posterior shoulder or indirect trauma in which the

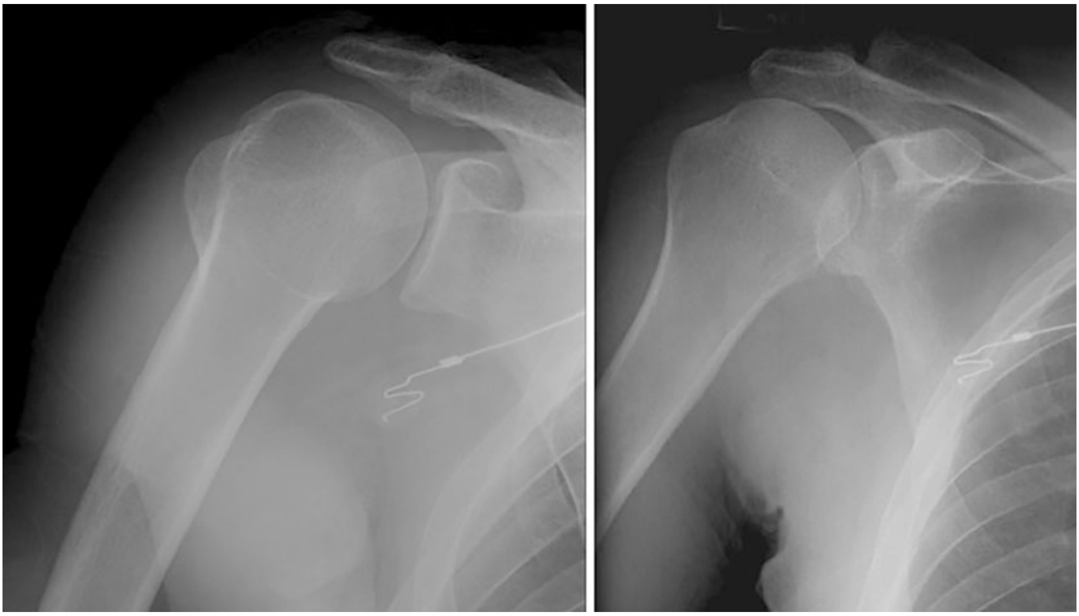

Fig. 25.2 Grashey and AP radiographs. AP radiograph is taken with the beam at 90° to the patient. The Grashey view is taken with the beam angled 30 degrees to be in line with the glenoid and proved a better view of the glenohumeral joint

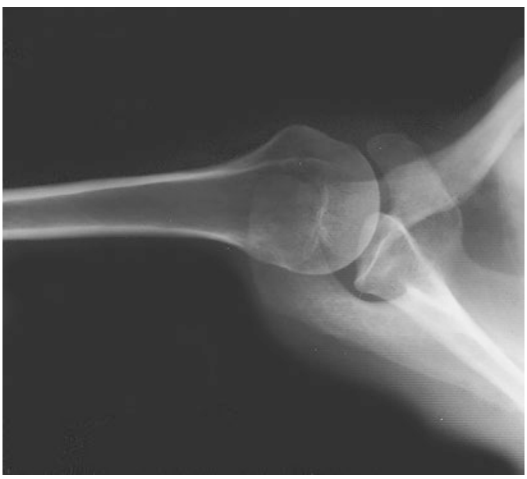

Fig. 25.3 Axillary radiograph. The axillary view is taken with the arm abducted from the body and the beam directly above the shoulder

arm is excessively abducted, extended, and externally rotated. Electric shock, seizures, or convulsions are much less common causes.

Patients typically present with the shoulder held slightly abducted and externally rotated. On exam there is a relative hollow posteriorly and laterally with a prominent acromion and palpable humeral head anteriorly (see Figs. 25.4 and 25.5). It is important to assess the integrity of the axillary and musculocutaneous nerves as these may suffer traction injuries. Patients will be unable to actively abduct the arm, but one should test sensation over the lateral shoulder [1].

The first step in treatment is closed reduction. Pain control may be obtained with sedation, analgesics, or intra-articular block. There are multiple reduction techniques described, which include the application of traction and gentle rotation to allow the humeral head to slide back into place (see Table 25.2). Acute dislocations that are unable to be reduced should be taken to the OR for open reduction as this is likely due to interposed soft tissue. After reduction the arm is immobilized in a sling for 2–5 weeks. Therapy should be started after immobilization is discontinued with progression of range of motion [1].

Recurrent pain and instability may result after a glenohumeral dislocation. 80–90% of patients under 20 with first-time dislocation will dislocate again, in comparison to 60% of patients under 30 and 10–15% of patients under 40. Indications for

Fig. 25.4 AP view of an anterior shoulder dislocation. AP view demonstrates the humeral head displaced inferiorly from the glenoid

surgical stabilization include first-time dislocation in highly active patients or athletes, soft tissue interposition that prevents reduction, greater tuberosity fracture that remains more than 5 mm displaced after reduction, or glenoid rim fracture greater than 5 mm. Surgical options include repair of labral tears, capsulorrhaphy, muscle or tendon transfers, or bony transfers in more refractory cases [1].

25.3.2 Posterior Dislocations

Posterior dislocations account for approximately 4% of shoulder dislocations, and up to 60–80% are missed on initial evaluation. The most common mechanism of injury is indirect trauma with the arm in adduction, flexion, and internal rotation. Direct force applied to the anterior shoulder may also cause posterior dislocation of the humeral head. Electric shock or convulsions in the setting of seizures or drug reactions may lead to posterior dislocation due to greater force of muscles of internal rotation (latissimus dorsi, pectoralis major, and subscapularis) compared to the external rotators (infraspinatus and teres minor) [1]. Given their infrequent occurrence, posterior shoulder dislocations can be missed by treating physicians.

Fig. 25.5 Axillary view of an anterior shoulder dislocation. Axillary view demonstrates anterior displacement of the humeral head

Table 25.2 Anterior shoulder dislocation reduction maneuvers

Technique	
Traction-countertraction	The patient is supine. Countertraction is applied with a sheet or towel in the affected axilla. The arm is abducted 45 degrees and traction is applied
Hippocratic technique	This is performed by one person. One foot is placed in the affected axilla, and gentle traction is applied to the arm with slight internal and external rotation
Stimson technique	Patient is placed prone on the table and the affected extremity allowed to hang free. Gentle traction toward the floor is applied, or a 5 lb. weight is applied to the wrist. Reduction can be expected in 15–20 minutes
Scapular manipulation	Patient is placed prone, and the inferior tip of the scapula is pushed medially and inferiorly, while the superomedial scapula is held stable
Milch technique	Patient is supine with the arm abducted and externally rotated, and hand or thumb pressure is used to push the humeral head into place
Kocher maneuver	The humeral head is levered against the glenoid to force reduction. This is not recommended due to chance of fracture

Clinically patients present with the arm held in internal rotation and adduction. There is less visible deformity than anterior dislocation. A palpable mass in the posterior shoulder and slight flattening of the anterior shoulder may be appre-

ciated. A complete neurovascular exam must be performed including evaluation of the axillary nerve. Traction injuries are less common but may occur. Exam will demonstrate limited external rotation and forward elevation. It is important to obtain a complete series of shoulder radiographs including the orthogonal axillary or Velpeau views as the abnormality may be very subtle on standard AP radiographs.

The first step in treatment is closed reduction. Posterior dislocations are typically more painful than anterior dislocations and commonly require full sedation or general anesthesia for adequate pain control and relaxation. The reduction is performed with the patient supine and application of traction in line with the adducted arm and gentle lifting of the humeral head [1]. Radiographs should be obtained to confirm adequate reduction. Patients should then be immobilized in a sling or external rotation brace for added stability.

Surgical stabilization is indicated in the setting of displaced lesser tuberosity fracture, large posterior glenoid fracture, irreducible dislocation, or significant impaction fracture on the posterior glenoid or anterior humeral head (reverse Hill-Sachs).

25.4 Proximal Humerus Fractures

Proximal humerus fractures account for 4–6% of all fractures and 45% of fractures of the humerus. Over 300,000 occur per year, making proximal humerus fractures more common than hip fractures. These injuries occur in a bimodal distribution with fragility fractures after low-energy trauma such as a ground-level fall onto outstretched arm in patients over 60 accounting for 75% and younger patients with high-energy mechanisms accounting for the remainder with a 2:1 female-to-male predominance [1, 2].

Patients typically present with the arm held closely to the chest and significant pain, swelling, and ecchymosis, severe pain, and crepitus with range of motion. It is important to perform a careful neurovascular exam, specifically to assess axillary nerve function and sensation over the lateral arm, as deltoid motor function is often limited by pain (Egole). It is important to obtain a full series of radiographs including an axillary or Velpeau view to rule out associated glenohumeral dislocation (see images 6 and 7). CT may be used to better evaluate articular involvement, displacement, and associated glenoid rim fractures [1].

The most commonly used classification system is the Neer classification in which the proximal humerus is divided into four parts: the greater and lesser tuberosities, humeral shaft, and humeral head and fractures are classified based on the number and displacement of parts. A part is defined as displaced if there is >1 cm of displacement or 45° of displacement. One-part fractures demonstrate no displacement, regardless of the number of fracture lines. The AO classification creates 27 types of fractures and is based on understanding of blood supply to the humeral head but is less commonly used. All classification systems have been shown to have poor interobserver reliability which limits their clinical usefulness [2].

The majority of these fractures occur in low-demand elderly patients and can be treated nonoperatively with immobilization in a sling until pain improves. Patients begin range of motion as soon as pain improves. These fractures are commonly seen to settle or displace throughout the healing process, but malunions are typically well tolerated in older, lower-demand patients.

Surgical treatment is indicated in younger more active patients or fractures with severe comminution or intra-articular involvement. Open reduction and internal fixation are indicated in patients with significantly displaced greater or lesser tuberosity fractures, displaced or unstable surgical neck fractures, and displaced and reconstructible three- and four-part fractures in younger patients. Arthroplasty with a total shoulder, reverse total shoulder, or hemiarthroplasty is indicated for patients with articular fracture comprising more than 40% of the articular surface, several comminuted fractures, or displaced of dislocated fractures in which blood supply to the humeral head is a concern. The goal of any surgical treatment is to optimize

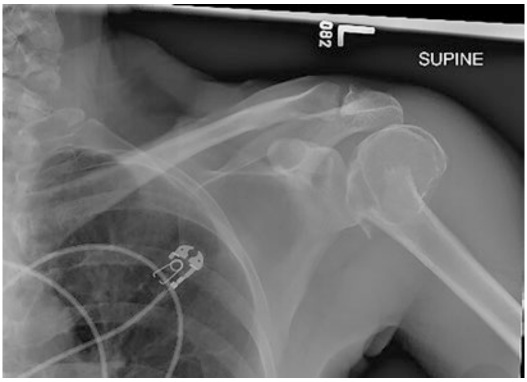

Fig. 25.6 AP view of left proximal humerus fracture. Radiographs of a left proximal humerus fracture after a ground-level fall in a 55-year-old female

Fig. 25.7 Axillary view of left proximal humerus fracture. Radiographs of a left proximal humerus fracture after a ground-level fall in a 55-year-old female

function while limiting morbidity and soft tissue damage [3].

Figures 25.6 and 25.7 show an AP and axillary view of a left proximal humerus fracture.

25.5 Humeral Shaft Fracture

Humeral shaft fractures account for 3–5% of all fractures with an incidence of 14.5/100,000 per year. They occur in a bimodal distribution with the highest incidence in men in their 20s and women in their 70s to 80s. Up to 10% of these fractures are open. Sixty percent of fractures involve the middle third, 30% the proximal third, and 10% of the distal third [3].

The most common mechanism of injury is direct trauma to the arm as in a motor vehicle accident, resulting in a transverse or comminuted pattern. Indirect trauma such as a fall on an outstretched arm resulting in a spiral or oblique pattern. Muscular attachments lead to typical patterns of displacement with the rotator cuff and deltoid pulling the proximal fragment into abduction and the biceps and triceps adducting the distal fragment, resulting in varus angulation [1].

Patients will present with pain, swelling, ecchymosis, deformity, crepitus, and shortening of the affected arm. It is important to carefully expect the skin, and any abrasions or lacerations must be examined carefully for evidence of open fracture. A careful neurovascular exam must be performed with particular attention to the radial nerve as it is in close proximity to the humeral shaft and is commonly injured. AP and lateral radiographs should be obtained as well as dedicated images of the shoulder and elbow joint to rule out intra-articular extension [1, 3] (see Figs. 25.8 and 25.9).

The goals of treatment are pain control, fracture union with acceptable alignment, and optimization of function. Up to 90% of fractures may be successfully treated nonoperatively with a coaptation splint encompassing the shoulder and elbow with transition to a functional brace in 1–2 weeks to allow swelling to subside. The functional brace utilizes compression of the soft tissues to stabilize the fracture and maintain alignment. The large range of motion and non-weightbearing status of the upper extremity allow the humerus to tolerate significant deformity without functional impairment. Fractures suitable for nonoperative management include AP angulation less than 20°, varus-valgus angulation less than 30°, and less than 3 cm of shortening [3].

Absolute surgical indications include open fractures with contamination or significant soft tissue damage, vascular injury, and compartment syndrome. Relative indications include polytrauma to allow earlier mobilization, bilateral upper extremity injuries, floating elbow injuries with both humeral and forearm fractures, severe soft tissue injury that precludes bracing, or artic-

Fig. 25.8 Right humeral shaft fracture. AP radiograph of a right humeral shaft fracture after placement of a coaptation splint. Not characteristic varus and anterior angulation at the fracture site

Fig. 25.9 Right humeral shaft fracture. Lateral radiograph of a right humeral shaft fracture after placement of a coaptation splint. Not characteristic varus and anterior angulation at the fracture site

ular involvement. Radial nerve palsy is not an indication for surgery, as the majority will resolve over time with observation. Fixation may be achieved via open reduction and internal fixation with a plate and screw construct, intramedullary nail, or external fixation depending on patient and fracture characteristics [3].

25.6 Impingement and Subacromial Bursitis

Subacromial impingement is the most common cause of atraumatic shoulder pain and accounts for 44–65% of shoulder disorders [3]. It is a category that encompasses a spectrum of pathology from subacromial bursitis to full-thickness rotator cuff tears. Impingement is described as a combination of intrinsic and extrinsic compression. Extrinsic compression describes compression of the humeral head by the anterior acromion, coracoacromial ligaments, and acromioclavicular joint. Acromion morphology may contribute significantly to impingement. Intrinsic compression is due to degeneration and thinning of the supraspinatus which allows the humeral head to migrate superiorly into the subacromial space. Repetitive contact and impingement of the soft tissues lead to inflammation, particularly of the subacromial bursa which decreases the bursa ability to minimize friction and lead to further inflammation.

Patients present with an insidious onset of shoulder pain exacerbated by overhead activity and lifting heavy objects away from the body. On physical exam, these patients typically have normal strength and positive findings on impingement tests. A positive Neer impingement sign

describes pain caused by passive forward elevation of the arm greater than 90°. A Hawkins test is positive if passive forward elevation to 90° and internal rotation cause pain. A positive Jobe test describes pain with resisted pronation and forward flexion to 90° and is indicative of supraspinatus pathology. An internal impingement test is positive with pain on abduction and external rotation of the shoulder [4].

Imaging is helpful to eliminate other sources of pain. Radiographs may demonstrate proximal migration of the humeral head due to rotator cuff arthropathy, subacromial spurring, calcification of the coracoacromial ligament, abnormal acromion morphology or os acromiale, and cystic changes of the greater tuberosity. MRI is used to evaluate for rotator cuff pathology and inflammation of the subacromial or subdeltoid bursa. Ultrasound can also be used to image the rotator cuff tendons and muscle bellies.

Treatment is primarily nonoperative with NSAIDs, subacromial injections, and physical therapy. Physical therapy emphasizes rotator cuff strengthening and periscapular stabilization techniques as well as stretching and mobilization of tight, noncontractile tissues. Injections including corticosteroids and biologics including platelet-rich plasma. Surgical intervention is only considered in refractory cases and may include subacromial decompression or acromioplasty in which the anteroinferior surface of the acromion is shaved and smoothed to minimize impingement on the underlying tissues.

25.7 Rotator Cuff Tears

Rotator cuff tears are a very common orthopedic complaint and represent part of a spectrum including subacromial bursitis and impingement and culminating in rotator cuff arthropathy. Rotator cuff tears may be found in patients of all ages, but are most common in patients over the age of 50 with a reported prevalence of 13% of patients in their 50s and 50% of patients over 80 [2]. A significant number of people may have asymptomatic rotator cuff pathology.

The rotator cuff consists of four muscles, the supraspinatus, infraspinatus, subscapularis, and teres minor, and functions to provide stability to the glenohumeral joint as well as assist with active motion of the shoulder. The limited blood supply to this area leads to minimal ability to heal. Tears can be described and classified by size, location, number of muscles involved, shape of the tear, and amount of muscle retraction, atrophy, and fatty infiltration (Table 25.3) [2]. Injury to the rotator cuff may be caused by several different mechanisms. Chronic intrinsic degeneration, which is most common in elderly patients, is the result of age-related degeneration of the tissue. Alternatively, chronic impingement leads to inflammation of the bursa or tendon itself, ultimately leading to structural weakening and degeneration. Acute injuries may be seen in patients following trauma or a fall and represents the most common mechanism of injury in younger patients.

Table 25.3 Exam of the rotator cuff

Muscle	Function	Maneuver
Supraspinatus	Abduction	Jobe test: weakness with resistance with the arm held in 90° of abduction, 30° flexion in the scapular plane, and forearm pronation
Infraspinatus	External rotation	Weakness with external rotation with the arm adducted and the elbow flexed to 90°
Subscapularis	Internal rotation	Lift off (arm held internally rotated with the dorsum of the hand on the lumbar spine, patient is unable to "lift off" the hand) or belly press (patient presses hand into lower abdomen, positive if unable to maintain internal rotation and elbow drops back)
Teres minor	External rotation	External rotation lag sign (elbow held at the side and arm passively externally rotated, positive if arm drifts into internal rotation) Hornblower's sign (shoulder brought to 90° of abduction, 90° of external rotation, positive if patient unable to hold this position)

Due to the varying acuity of injury, patients will present with a variable history of symptoms. The majority of patients will report pain with activity, particularly worse with overhead activity. Patients with severe symptoms may report pain at night and rest. Patients will have limited active range of motion, but normal passive range of motion in contrast to adhesive capsulitis. Patients will have weakness with isolated muscle function testing (see Fig. 25.3).

Imaging should begin with plain radiographs which may demonstrate joint space narrowing or sclerosis consistent with arthritic changes to the glenohumeral or acromioclavicular joints and superior migration of the humeral head due to chronic atrophy of the supraspinatus. Ultrasound may be used to assess the integrity of the tendons and presence of effusion. MRI is the gold standard for diagnostic imaging and will demonstrate location, size, and shape of a tear as well as condition of the muscle, amount of tendon retraction, and presence of other pathology that may need to be addressed at the time of surgery.

The first step in management, particularly for chronic injuries, is nonsurgical, consisting of rest, avoidance of exacerbating activity, NSAIDs, subacromial injections, and physical therapy focusing on range of motion and strength of scapular stabilizing muscles and rotator cuff musculature. Younger and more active patients may be considered for repair. The majority can be treated arthroscopically. Acute tears without significant tissue atrophy may be candidate for direct repair, while larger or more chronic tears may require tendon transfers to restore function. Postoperative rehabilitation is based on size and complexity of the tear and patient characteristics with the goal of returning to full activity with normal strength and range of motion [2].

25.8 Calcific Tendinitis

Calcific tendinitis is a condition of calcification and degeneration of a tendon of the rotator cuff. This condition most commonly affects the supraspinatus and is associated with subacromial impingement. The most commonly affected patients are women between 30 and 60, with patients with diabetes and hypothyroidism most at risk. The ultimate cause is not entirely understood.

There are three stages to this process beginning with painless pre-calcific stage in which there is fibrous metaplasia of the tendon. The calcific phase begins with a formative period in which calcium hydroxyapatite crystals are deposited, followed by a resting phase and then a resorptive phase defined by resorption by phagocytes and vascular infiltration. The early calcific phase may not be painful, but the resorptive phase is reliably the most painful. The process culminates with the post-calcific phase. Classification systems are based on size, shape, and density of the deposits.

Patients will present with atraumatic pain with similar history to subacromial impingement. They may report symptoms of catching, crepitus, or mechanical block to motion. Patients will have pain with subacromial impingement tests, as well as decreased active range of motion with variable changes in rotator cuff strength.

Plain radiographs are the best imaging modality for calcific tendinosis. The deposits will be visible, and serial radiographs will allow monitoring of progression over time. Different views are preferred for varying locations. Calcification of the supraspinatus is seen in AP and axillary views; calcification of the infraspinatus and teres minor is seen with internal rotation views and subscapularis seen on external rotation view. MRI is not necessary for diagnosis, but may be useful in patients with refractory pain or nonspecific exam findings to rule out concomitant rotator cuff tear or labral injury.

Treatment is primarily nonoperative with NSAIDs, physical therapy for stretching and strengthening, and possible steroid injections. 60–70% of patients have relief of symptoms within 6 months. Conservative management is less likely to be successful with bilateral or large calcifications, deposits beneath the anterior third or medial to the acromion. Supplementary modalities include extracorporeal shock-wave therapy and ultrasound-guided needle lavage in which two needles are inserted into the deposit

with one used for injection of saline and the other used for aspiration of deposits or corticosteroid injection directly into the deposit in patients with more severe or refractory cases. Surgical debridement of the calcium deposit may be indicated for refractory cases with continued progression and interference with activity [2, 4].

25.9 Superior Labrum Anterior to Posterior (SLAP) Tears and Bicipital Tendinitis

Superior labrum anterior to posterior tears with or without involvement of the long head of the biceps are relatively uncommon injuries to the shoulder. This injury is most commonly seen in overhead and throwing athletes as a result of repetitive activity, but may also occur after fall on outstretched arm or traction injury. They are commonly associated with internal impingement, glenohumeral internal rotation deficit, rotator cuff tears, shoulder instability, or scapular dyskinesia.

The glenoid labrum is a ring of fibrocartilage that surrounds the glenoid fossa and serves to deepen the joint socket. The blood supply to the labrum enters peripherally from the suprascapular artery, circumflex scapular artery, and posterior humeral circumflex artery. The innermost ring of the labrum is relatively avascular. The superior labrum attaches just medial to the articular surface of the glenoid rim at the supraglenoid rim. The long head of the biceps tendon typically shares this insertion, splitting attachment on the supraglenoid tubercle and superior labrum before passing intra-articularly through the glenohumeral joint and exiting in the bicipital groove [2].

Proximal biceps tendon can also be a significant source of pain, but is difficult to isolate as it is usually associated with other conditions. Biceps pathology can include tendinitis, tears, subluxation, entrapment, delamination, and dislocation out of the bicipital groove. Subscapularis tears are associated with LHB tendon instability as the subscapularis serves as a restraint to the tendon in the bicipital groove.

SLAP tears may be acute or chronic. Acute tears are caused by traction or direct compression. Chronic tears are caused by chronic overhead activity. The Snyder classification is most commonly used to describe these injuries. Type I is defined as fraying and local degeneration of the superior labrum, while the labrum and biceps insertion remain intact. Type II lesions involve detachment of the superior labrum and biceps insertion from to the glenoid, allowing abnormal movement, and are the most common. Type III tears involve a bucket handle tear of the superior labrum with an intact insertion for the long head of the biceps, while in type IV lesions, the tear extends to the insertion of the LHB. A type V tear describes a SLAP tear associated with a Bankart lesion. A type VI lesion is a combination of SLAP and unstable labral tear, while a type VII tear extends to the origin of the medial glenohumeral ligament [2].

Patients with SLAP tear of tendinopathy of the long head of the biceps will present with similar symptoms to other shoulder problems with pain and decreased range of motion. No single exam maneuver is diagnostic of a SLAP tear, although the Speed test (resisted forward elevation of an extended arm and supinated forearm) and Yergason test (elbow is flexed to 90° and held at the patient's side, and patient supinates forearm against resistance) are more specific for biceps pathology and are often positive in patients with SLAP tears. Tenderness in the bicipital groove may be present in biceps tendinitis. In cases of biceps instability, the tendon may be able to be dislocated or reduced in the groove [2].

Plain radiographs should be taken to look for other sources of pathology of the glenohumeral or acromioclavicular joints. MRI allows visualization of the biceps tendon, bicipital groove, and rotator cuff. MRI arthrogram allows better visualization of the labrum. Ultrasound is useful for assessing subluxation or dislocation of the LHB tendon and can be used for dynamic stress testing in the setting of a questionable diagnosis. The gold standard of diagnosis is arthroscopy.

Nonsurgical treatment in the form of physical therapy focusing on posterior capsular stretching and rotator cuff and scapular stabilizer strength-

ening, NSAIDs, and intra-articular steroid injections or injections into the biceps tendon itself can provide significant improvement in symptoms of SLAP tears and biceps tendinitis. Surgery is considered when 3 months of conservative management have failed. Surgery may involve repair of the SLAP lesion, biceps tenotomy, or biceps tenodesis in which the insertion of the LHB is detached from the labrum and supraglenoid tubercle and reinserted onto the humerus. Patients under 40 are likely to receive more benefit from SLAP repair than tenodesis. Both tenodesis and tenotomy are options in older patients.

25.10 Glenohumeral Osteoarthritis

Osteoarthritis of the glenohumeral joint is a chronic degeneration of the articular surface of the joint resulting in loss of cartilage and incongruence of the joint. Incidence and severity increase with advancing age, although symptoms may begin as early as the fourth or fifth decade. There are many underlying causes. Primary osteoarthritis has no known cause. Inflammatory arthritis is caused by disease processes such as rheumatoid arthritis or autoimmune disease. Posttraumatic arthritis can occur after chronic dislocations, repetitive injury, or fracture. Osteonecrosis of the humeral head occurs after disruption of blood supply to the humeral head as in proximal humerus fractures, chronic steroid or alcohol abuse, or hemoglobinopathies such as sickle cell disease. Rotator cuff arthropathy is due to an insufficient rotator cuff leading to altered joint mechanics and superior migration of the humeral head. Crystalline arthropathy is due to repeated episodes of gout or pseudogout leading to deposition of sodium urate or calcium pyrophosphate crystals.

Patients with arthritis have progressive shoulder pain that is worse with activity and improved with rest as well as decreased range of motion and crepitus. Patients will typically report difficulty sleeping. Physical exam will demonstrate a limited range of motion in all planes. There may be palpable or audible crepitus, catching, or squeaking. It is important to assess integrity of the rotator cuff which is important in determining treatment options, as well as radiating pain from a cervical spine problem.

Radiographs are the most important imaging study for the diagnosis of arthritis. Images will demonstrate joint space narrowing, subchondral cysts and sclerosis, osteophytes, and possible humeral head subluxation. Patients with inflammatory arthritis will exhibit minimal osteophytes, significant osteopenia, and marginal erosions of the humeral head. In the case of crystalline arthropathy, there may or may not be radiopaque calcific deposits. MRI and CT are rarely indicated (see Fig. 25.10).

Nonoperative management is the mainstay of treatment with physical therapy to improve range of motion and strength, NSAIDs, and intra-articular steroid injections, as well as medical management of underlying conditions including rheumatoid arthritis, gout, and hemoglobinopathies. Arthroscopic debridement of loose bodies or hyperplastic synovium may provide pain relief as well as improve range of motion in mild cases. Arthroplasty is indicated for end-stage arthritis that has failed all nonoperative management. Total shoulder arthroplasty is an option for patients with intact rotator cuff. Reverse total shoulder arthroplasty is useful for patients with large or irreparable rotator cuff tear or severe glenoid wear and is becoming a more and more

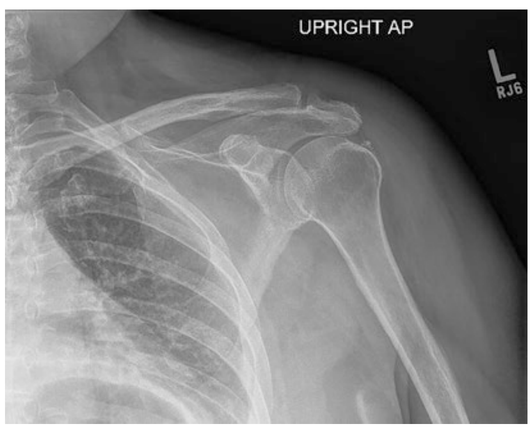

Fig. 25.10 Left glenohumeral osteoarthritis. AP radiograph of a left shoulder with glenohumeral osteoarthritis. Note significant joint space narrowing and superior migration of the humeral head

popular option. Hemiarthroplasty is an option for younger patients or patients with rheumatoid arthritis and poor bone quality, but is becoming less popular as results are not as good as TSA or reverse TSA. In the case of paralysis, Charcot arthropathy, or chronic infection, arthrodesis in which the shoulder is fused in a functional position may improve pain and function. The goal of arthroplasty is to provide lasting pain relief and improvement in function, and with today's implants, 10-year survival is as high as 95% [4].

25.11 Adhesive Capsulitis

Adhesive capsulitis, or frozen shoulder, describes a disorder of atraumatic onset of shoulder pain and progressive decrease in shoulder range of motion caused by inflammation and fibrosis. There is typically no identifiable cause, although it may be associated with diabetes or thyroid disease. Although often debilitating, and symptoms can take a significant period of time to resolve, the condition usually resolves.

Patients will present with a history of sudden onset of diffuse shoulder pain and progressive loss of shoulder range of motion. The most significant exam finding is significant decrease in both passive and active range of motion. It is important to rule out other causes of pain including rotator cuff or labral pathology, osteoarthritis, or radiating pain from the cervical spine. MRI and radiographs may be obtained to rule out other causes of pain.

Treatment is almost entirely nonsurgical with physical therapy and exercise. NSAIDs and intra-articular corticosteroid injections may also be helpful. Adjunctive but less commonly used treatment options include electrotherapy, extracorporeal shock-wave therapy, suprascapular nerve stimulation, and distention arthrography in which the joint capsule is distended with corticosteroids or saline. Surgical treatment is rarely indicated but may include manipulation under anesthesia or capsular release. The majority of cases will resolve with sufficient time.

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26 Common Clinical Conditions of the Elbow

Daniel Carpenter and Reid W. Draeger

Contents

Goals and Objectives

- *Goal*: To introduce the reader to common musculoskeletal clinical conditions of the elbow
- *Objectives*: On completion of this unit, and using the syllabus as a standard reference, the learner should be able to describe and define the:
  1. Differing characteristics and possible treatments for fractures and dislocations about the elbow
  2. The symptoms, exam findings, and treatment options for cubital tunnel syndrome

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3. Common tendinitis of the elbow and treatment options for these
4. Ligamentous injuries about the elbow that can lead to instability and their possible treatment options
5. Etiologies of arthritis about the elbow and treatment options for elbow arthritis

26.1 Elbow Anatomy

The elbow is a highly complex and congruent joint formed by the distal humerus and the proximal radius and ulna bones of the forearm. The distal humeral articular surface is formed by the trochlea medially and the capitellum laterally which articulate with the proximal ulna and radius, respectively (Fig. 26.1a). The ulnohumeral articulation forms the primary hinge component of the joint allowing flexion and extension of the elbow. The radiocapitellar and proximal radioulnar joints work in concert to facilitate forearm pronation and supination as well as to confer further bony stability (Fig. 26.1b). Though the highly congruent bony architecture of the elbow yields significant intrinsic stability, the surrounding soft tissues remain crucial in providing both static and dynamic support of a stable joint. The static structures include primarily the medial and lateral collateral ligaments and the joint capsule. The dynamic structures are the various muscle groups crossing the elbow. Normal range of motion of the elbow is from approximately 0° (full extension) to 140° (full flexion) [1]. Normal limits of supination and pronation are around 90° and 85°, respectively. Functional range of motion for activities of daily living has traditionally been described as flexion from 30° to 130° and supination and pronation of both 50° [2]. Major neurovascular structures traversing the elbow include the brachial artery and the median, radial, and ulnar nerves.

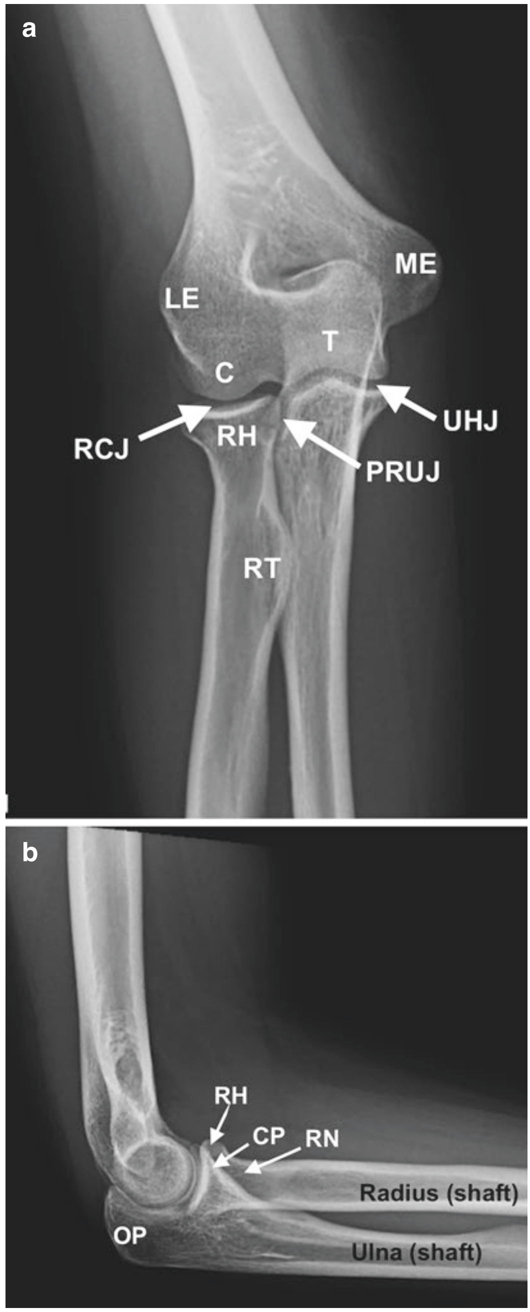

Fig. 26.1 Elbow bony anatomy. (**a**) Normal anterior-posterior (AP) radiograph of the elbow. Lateral epicondyle of the humerus (LE), medial epicondyle of the humerus (ME), capitellum of the humerus (C), trochlea of the humerus (T), radial head (RH), radial tuberosity (RT), ulnohumeral joint (UHJ), radiocapitellar joint (RCJ), and proximal radioulnar joint (PRUJ). (**b**) Normal lateral radiograph of the elbow. Coronoid process of proximal ulna (CP), olecranon process of proximal ulna (OP), radial head (RH), radial neck (RN), radial shaft, and ulnar shaft

26.2 Elbow Trauma

26.2.1 Distal Humerus Fractures

Adult fractures of the distal humerus in adults are relatively uncommon but often severe injuries. Though several classifications exist, these fractures can broadly be classified based on articular (joint surface) involvement and partial or complete involvement of both medial and lateral condyles (Fig. 26.2) [3]. These injuries are typically seen in a bimodal age distribution – in young patients after high-energy trauma and in elderly patients as a low-energy, osteoporotic fracture. Initial management of these injuries includes a detailed neurovascular exam and provisional reduction and immobilization. Nonoperative management is uncommon but possible in minimally displaced fractures and in patients with low functional demand. This would typically entail a period of cast or splint immobilization which can result in significant loss of motion. The mainstay of treatment is surgical open reduction and internal fixation. Depending on fracture pattern, this can be accomplished with either medial plating, lateral plating, or a combination of medial and lateral plates (Fig. 26.2). The primary goal of open reduction internal fixation is to restore the congruity of the articular surface with stable fixation so as to allow early elbow motion. Common complications include wound breakdown, elbow stiffness, post-traumatic arthritis, ulnar neuropathy, and heterotopic ossification. For severely comminuted fractures in elderly patients, total elbow arthroplasty (replacement) is an option with good results (Fig. 26.3) [4]. Treatment of these often complex injuries will be based on the pattern of the fracture as well as the age and functional demands of the patient. With appropriate treatment, good functional outcomes can be expected.

26.2.2 Olecranon Fractures

The olecranon is the most proximal portion of the ulna that articulates with the humerus forming the ulnohumeral joint. Fractures involving the olecranon are relatively common across all age groups and typically result from a fall onto or direct blow to the posterior elbow. The triceps tendon inserts onto the olecranon process and is thus the primary force causing fracture diastasis or separation. Because these are intra-articular and often displaced fractures, the recommended treatment is typically open reduction and internal fixation. A variety of fixation techniques are used and include plating, screw fixation, and tension band constructs (Fig. 26.4). Fixation technique is often chosen based on surgeon preference and the

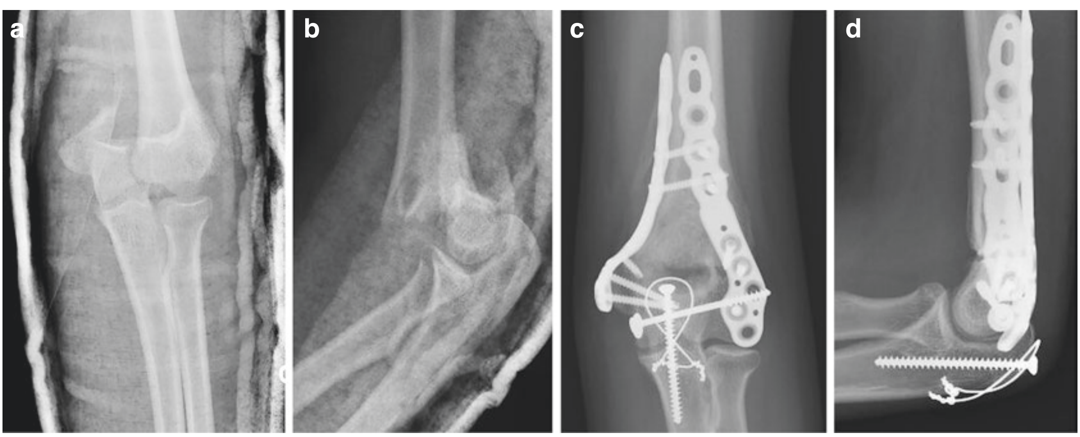

Fig. 26.2 Distal humerus fracture. (**a**) AP and (**b**) lateral radiographs of bicondylar, intra-articular distal humerus fracture with overlying splint material. (**c**) AP and (**d**) lateral radiographs of open reduction internal fixation with plate and screw construct. To gain exposure to the articular surface during fixation, an olecranon osteotomy is often performed. A tension band construct securing the osteotomy is seen on the proximal ulna

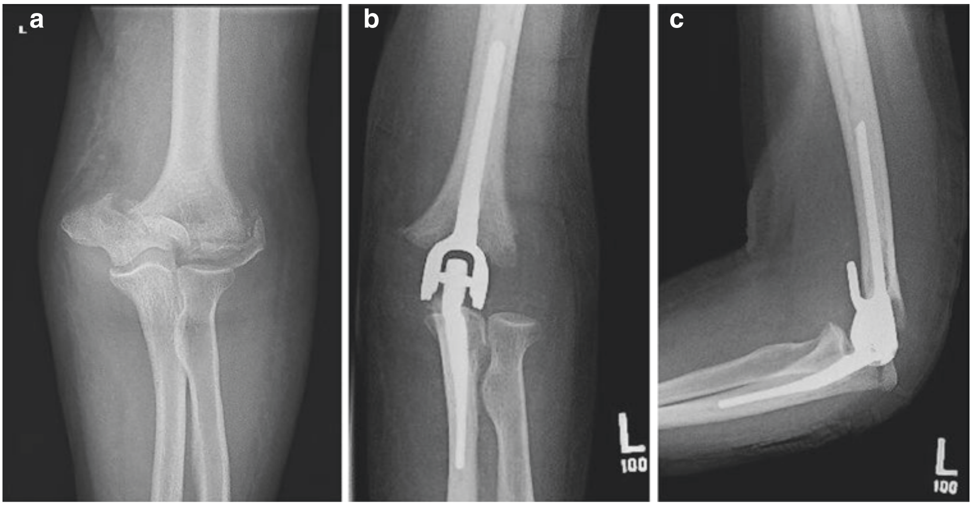

Fig. 26.3 Comminuted distal humerus fracture. (**a**) AP radiograph of extensively comminuted fracture of the distal humerus in an 80-year-old patient. Given the fracture pattern and patient age, the fracture was treated with total elbow arthroplasty. (**b**) AP and (**c**) lateral radiographs of semi-constrained total elbow arthroplasty

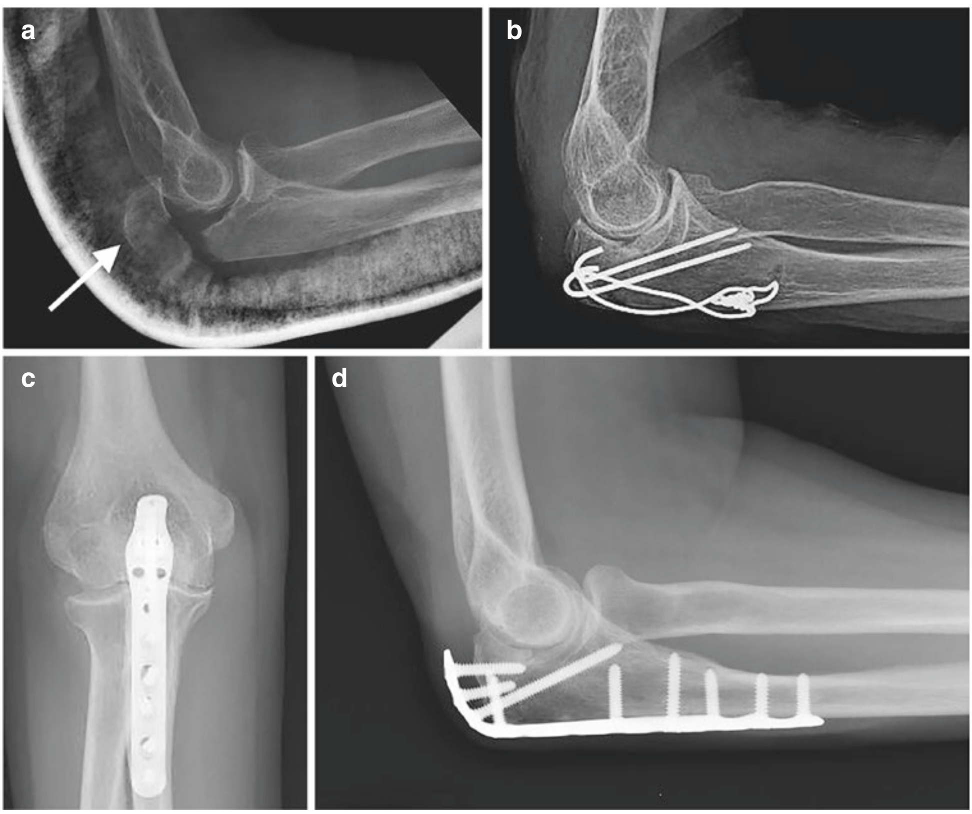

Fig. 26.4 Olecranon fractures. (**a**) Lateral radiograph of the elbow with displaced olecranon fracture with proximal retraction of the olecranon process (arrow). Overlying splint material is also seen. (**b**) Tension band construct with healing of the fracture is seen 2 months after surgery. (**c**) AP and (**d**) lateral radiographs of plate and screw fixation of a similar fracture

characteristics of the fracture. Comminuted fractures are more likely to be fixed with a plate and screw construct, whereas simple or transverse fracture patterns are more amenable to tension band or only screw constructs [5]. Nonoperative management is sometimes possible in patients with low functional demand and has been reported with satisfactory results in this population [6]. This treatment would typically involve a short period of splint or cast immobilization followed by early motion [6]. The most common complication following surgical fixation is symptomatic hardware given the subcutaneous nature of the olecranon and thus hardware. Other complications include wound breakdown, elbow stiffness, and heterotopic ossification [5]. Nonetheless, with appropriate treatment most patients have good functional outcomes with minimal long-term functional deficits.

26.2.3 Radial Head Fractures

Fractures of the radial head are relatively common and represent up to an estimated 33% of adult elbow fractures. They typically occur after a fall on an outstretched arm [7]. These injuries can occur either in isolation or in association with an elbow dislocation (see elbow dislocations). The radial head acts as an important stabilizer of the elbow, particularly to valgus stress. The radial head also confers longitudinal stability to the forearm through the radiocapitellar articulation [8]. Injury can result in many fracture patterns ranging from non-displaced to displaced and comminuted. The Mason classification is often used to help categorize displacement and fracture pattern and can thus guide treatment [9]. Mason Type 1 fractures are non-displaced or minimally displaced (<2 mm), and nonoperative treatment is recommended. This involves a short period of immobilization followed by early range of motion of the elbow. Mason Type 2 fractures have >2 mm of fracture displacement or angulation. If the fracture does not block motion of the elbow, then nonoperative management is possible (Fig. 26.5). For fractures with a mechanical block and significant displacement, open reduction and internal fixation are recommended (Fig. 26.5). Mason Type 3 fractures have significant comminution. These fractures are typically treated with radial head arthroplasty (replacement) (Fig. 26.5). Radial head excision is an option for severely comminuted fractures though is generally not a good option if concomitant ligamentous or other bony injuries exist [10]. Minimally displaced radial head and neck fractures that occur in isolation generally have good results with nonoperative management. More complex injuries to the radial head and neck rarely occur in isolation, and a systematic approach must be taken in

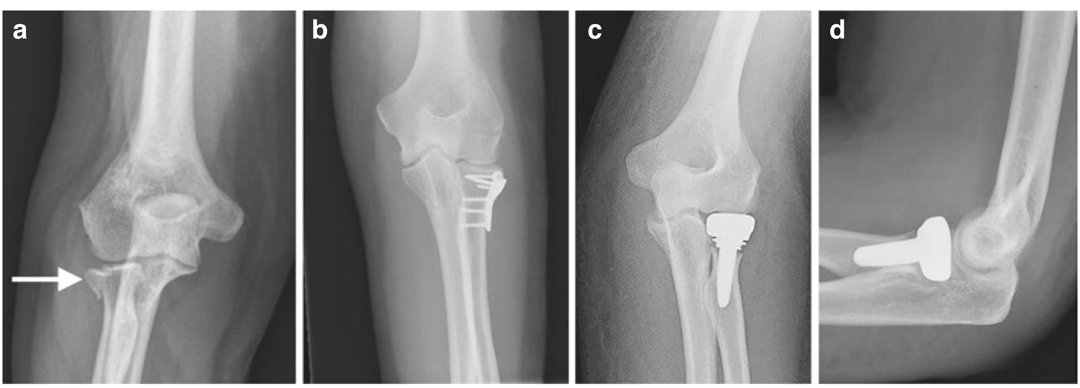

Fig. 26.5 Radial head fractures. (**a**) AP radiograph of minimally displaced radial head fracture (arrow). This patient was treated with nonoperative management and had return of full, painless range of motion 2 months after the injury. (**b**) AP radiograph of a more displaced radial head fracture treated with open reduction internal fixation. (**c**) AP and (**d**) lateral radiographs of radial head replacement

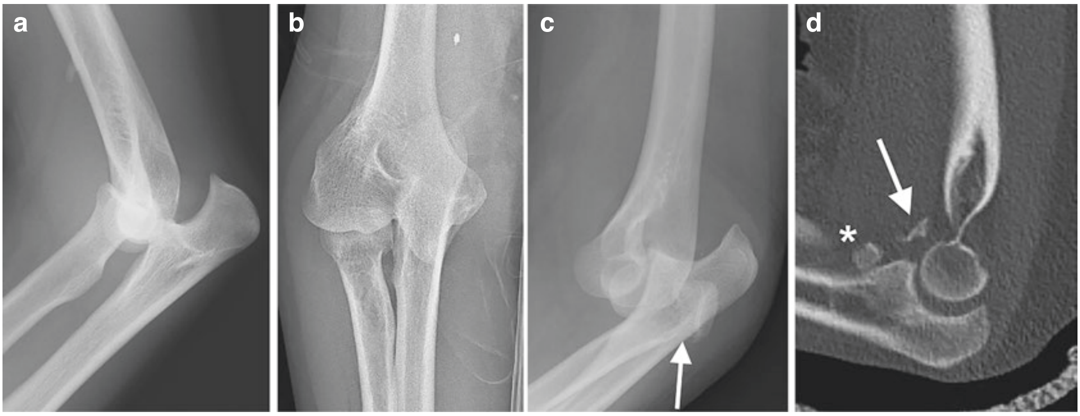

Fig. 26.6 Simple and complex elbow dislocations. (**a**) Lateral radiograph of simple posterior elbow dislocation without fracture. (**b**) AP and (**c**) lateral radiograph of complex "terrible triad" posterior dislocation. An angulated radial neck fracture can be seen on the lateral (arrow). (**d**) After reduction of the elbow, a CT scan demonstrates a small coronoid process fracture (arrow) and fragment of radial head (asterisk) (coronoid process fractures are often small and not seen on plain radiographs)

treating associated injuries. Complications following internal fixation include loss of fixation, nonunion, and radiocapitellar arthritis. Complications following radial arthroplasty include overstuffing the radiocapitellar joint and loosening of the prosthesis [7].

26.2.4 Elbow Dislocations

Elbow dislocations can be categorized as either simple or complex. Simple dislocations involve damage to capsular and ligamentous structures alone, whereas complex dislocations typically involve bony injury as well. As with other joints, an elbow dislocation is described by the direction of the distal segment (in this case olecranon and radial head) in relation to the proximal segment (humerus). A posterolateral direction of dislocation represents up to 85% of elbow dislocations and is most often the result of a fall onto an outstretched arm [11]. Simple elbow dislocations (Fig. 26.6) are initially managed with closed reduction under local or general anesthesia. Following reduction, the joint is typically immobilized in a splint or cast for several days followed by subsequent early motion. Though surgical treatment following simple elbow dislocations is uncommon, it can be necessary in cases of significant post-reduction instability or incarcerated small bony fragments in the joint. Neurovascular injury is rare, but nonetheless a thorough physical exam must be performed both prior to and following reduction. Complex elbow dislocations can be much more difficult to manage. One particular combination of injury has become known as the "terrible triad of the elbow." This involves an elbow dislocation, coronoid process fracture, and radial head fracture (Fig. 26.6) [12]. Following urgent reduction of the dislocation, these injuries typically require surgical intervention to address bony and ligamentous injury. Simple radial head fractures can be repaired, while more comminuted radial head fractures require replacement (see section on radial head fracture). Additionally, the coronoid process can be repaired with various techniques. To further augment stability, the torn lateral collateral ligament is also typically repaired. Though these "terrible triad" injuries have historically had poor outcomes, a systematic approach of addressing bony and ligamentous injury can lead to good outcomes [12]. Complications fol-

lowing this injury can include persistent instability, heterotopic ossification, elbow stiffness, and fracture nonunion [13].

26.2.5 Pediatric Supracondylar Humerus Fractures

Supracondylar humerus fractures are the most common elbow fracture in the pediatric population, most commonly occurring in the 5–7-year age group [14]. The typical mechanism of injury is a hyperextension of the elbow after a fall onto an outstretched arm (Fig. 26.7). An uncommon variant is a flexion-type injury which is typically the result of a fall onto a flexed elbow. The supracondylar humerus area is undergoing remodeling in this age group which results in a thinner area of bone prone to fracture [14]. The Gartland classification classifies extension-type fractures into four (I–IV) categories based on displacement of the fracture [15]. Type I injuries are minimally displaced and are typically treated nonoperatively with cast immobilization. Types II–IV are increasingly more displaced and are typically treated surgically. The mainstay of surgical treatment is closed reduction and percutaneous pin fixation under general anesthesia – usually within 24 h of injury (Fig. 26.7). Rarely an open incision will be necessary to aid in reduction of the fracture. Injuries associated with supracondylar humerus fractures can include neurological and vascular injuries as well as forearm compartment syndrome. The most common neurological injury in an extension type injury is an anterior interosseous nerve (AIN) neuropraxia that typically resolves with time [14]. Vascular injury to the brachial artery is rare but can necessitate vascular surgery intervention if extremity remains dysvascular following reduction. The most common late complication is malunion which can lead to a cubitus varus or "gunstock" deformity [16]. Though pediatric supracondylar humerus fractures are serious injuries with potentially severe complications, with proper management outcomes are typically good with little to no long-term disability.

26.3 Compression Neuropathy

26.3.1 Cubital Tunnel Syndrome

Cubital tunnel syndrome is compression or irritation of the ulnar nerve as it courses by the elbow. It is the second most common peripheral nerve compression syndrome following carpal tunnel syndrome [17]. After leaving the brachial plexus, the ulnar nerve courses along the medial arm and pierces the medial intermuscular septum. From here it courses posterior to the medial epicondyle as it crosses the elbow before traveling down the forearm. There are several areas of possible compression along its course about the elbow. The arcade of Struthers is a thickened band of tissue between the triceps and intermuscular septum and is the first possible area of compression. As the nerve passes posterior to the medial epicondyle, it traverses through the cubital tunnel proper which is covered by the ligament of Osborne. This represents the most common area of ulnar nerve compression [18]. Beyond the elbow into the forearm, the nerve can be compressed as it travels between the two heads of the flexor carpi ulnaris (FCU). Typical symptoms of cubital tunnel syndrome are exacerbated by elbow flexion beyond 90°. With deep elbow flexion, the space within the cubital tunnel significantly narrows and can further irritate an already compressed nerve [19]. These symptoms typically include altered sensation in the ulnar ring finger and entire small finger and weakness of the hand. Common exam findings are paresthesias and pain with percussion over the cubital tunnel (Tinel's sign) or elbow flexion with direct pressure of the cubital tunnel (pressure-flexion) test [20]. Weakness and atrophy of the intrinsic muscles of the hand can be seen in late or severe cases of cubital tunnel syndrome. Though physical exam is foundational to the diagnosis of ulnar nerve compression, definitive diagnosis can be confirmed with electrodiagnostic testing. For patients with mild to moderate symptoms, initial treatment is typically nonoperative and is often successful. This primarily involves nighttime extension bracing which limits elbow flexion and

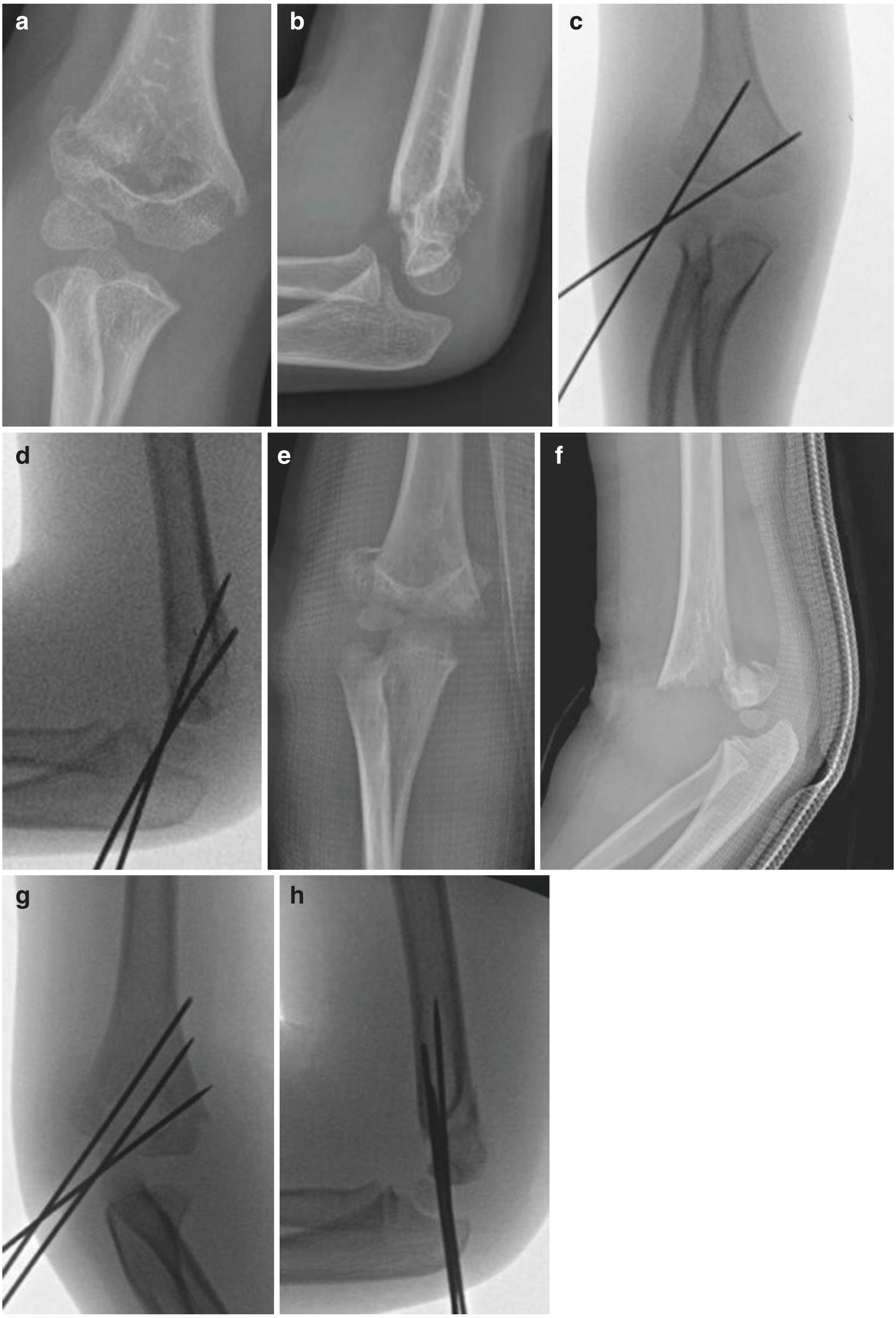

Fig. 26.7 Supracondylar humerus fractures. (**a**) AP and (**b**) lateral radiographs of a Gartland Type II supracondylar humerus fracture. (**c**) AP and (**d**) lateral intraoperative fluoroscopy views of percutaneous pin fixation. (**e**) AP and (**f**) lateral radiographs of a Gartland Type III supracondylar humerus fracture. (**g**) AP and (**h**) lateral intraoperative fluoroscopy views of percutaneous pin fixation

avoiding activity that involves periods of sustained elbow flexion or direct pressure on the posterior elbow [21]. For patients with severe weakness or significantly altered sensation and muscle atrophy, surgical management is typically employed. Surgical options include in situ decompression with release of offending structures, ulnar nerve transposition anterior to the medial epicondyle (subcutaneous or submuscular), and medial epicondylectomy. There are benefits and disadvantages to each approach though they overall have similar, favorable outcomes [17, 22]. Cubital tunnel syndrome represents a relatively common nerve compression syndrome, and with early and appropriate management, patients can expect excellent functional outcomes.

26.4 Tendinitis and Bursitis

26.4.1 Lateral Epicondylitis

Lateral epicondylitis, also known as "tennis elbow," is the most common tendinopathy of the elbow. It affects an estimated 1–3% of adults on a yearly basis and is thought to be a result of activities involving repetitive, resisted wrist extension. The pain generated is thought to be related to microtrauma and inflammation to the common wrist extensor origin at the lateral epicondyle of the humerus. More specifically, the extensor carpi radialis brevis (ECRB) has been implicated as the muscle most commonly involved. The diagnosis is typically made from history and physical exam, and imaging is often not indicated. Though the ideal treatment of lateral epicondylitis remains somewhat unknown, nonsurgical management is typically successful. Initial strategies include anti-inflammatory medication, activity modification, injections, physical therapy, and bracing. Brace options include either a forearm strap (also known as a counterforce brace) or a wrist extension brace. A forearm strap works to relieve stress on the lateral epicondyle by limiting muscle excursion and acting as a "secondary" muscle origin. A wrist extension splint acts to relieve tension on the wrist extensors and thus lateral epicondyle [23]. Corticosteroid injections have been studied at length and are thought to provide little to no long-term relief and are generally not recommended [24]. Though the vast majority of patients respond to nonoperative measures, occasionally surgery can be used for recalcitrant cases. This involves either open or arthroscopic debridement of the involved portion of the ECRB and has overall good results when necessary [25]. Though lateral epicondylitis or "tennis elbow" occurs with relative frequency in the general population, most patients will respond well to nonoperative treatment and will have full relief of symptoms within 6 months to 1 year [26].

26.4.2 Medial Epicondylitis

Medial epicondylitis, also known as "golfer's elbow," is similar in pathology and presentation to lateral epicondylitis but is related to the common flexor tendon originating from the medial epicondyle of the humerus. It is much less common than lateral epicondylitis and has an estimated prevalence of <0.5% [27]. Medial epicondylitis is thought to be related to activities involving eccentric loading of muscles involved with wrist flexion and forearm pronation. The pain produced is thus a result of microtrauma and inflammation to the common flexor pronator mass [28]. Rather than a purely clinical diagnosis, an MRI is often ordered to confirm the diagnosis of medial epicondylitis and will typically show increased signal within the common flexor tendon [29]. Other concomitant diagnoses are common and can include ulnar neuritis and valgus instability. As with lateral epicondylitis, initial treatments are typically nonoperative and include activity modification, anti-inflammatory medications, physical therapy, bracing, and injections. The majority of cases will respond well to nonoperative management. For recalcitrant cases, surgical management is possible which involves open debridement and repair of the involved tendon unit and also addressing concomitant pathology such as ligamentous injury or ulnar nerve compression.

26.4.3 Olecranon Bursitis

The olecranon (proximal ulna) has an overlying bursal layer that forms in response to direct pressure between the underlying bone and the shearing forces applied to the overlying skin during activity. This bursal tissue can become inflamed and collect fluid as a result of either infectious, traumatic, or inflammatory processes. The diagnosis of olecranon bursitis is typically made from physical exam and will demonstrate a subcutaneous fluid collection at the posterior elbow with possible overlying skin changes such as erythema. In cases of acute bursitis, it is important to differentiate between septic (infectious) and aseptic (non-infectious) causes of inflammation. Erythema, warmth, and pain can be present in both septic and aseptic bursitis though are more commonly seen in septic bursitis [30]. To further aid in diagnosis, an aspiration of the fluid collection can be performed with fluid analysis. A positive culture or gram stain along with increased white blood cell (WBC) count and decreased bursal fluid glucose levels would be indicative of a septic bursitis. A negative culture with low WBC count would be indicative of a noninfectious process. Management of olecranon bursitis varies based on the underlying pathology. For aseptic bursitis, nonoperative management is typically successful. This includes rest, compressive dressing, ice, anti-inflammatories, and activity modification. Steroid injection has been described as a successful treatment by some [31] though others report a relatively high rate of complication [32]. The treatment of confirmed septic bursitis is typically systemic antibiotic therapy and then incisional drainage or serial aspiration if no improvement on antibiotics alone. Surgical treatment must be undertaken cautiously as significant complications can result, most commonly related to wound healing [33]. One unique consideration when performing a posterior elbow incision is temporary elbow immobilization to facilitate wound healing as this area can be prone to breakdown from mechanical stresses during elbow flexion [34]. Other noninfectious cases of olecranon bursitis can be due to rheumatoid arthritis, gout, and underlying bone spurs. In summary, olecranon bursitis can be due to both aseptic and septic causes and typically responds well with appropriate and most often nonsurgical treatment.

26.5 Ligamentous and Tendinous Injury

26.5.1 Lateral and Medial Collateral Injury

As previously mentioned, the ligaments of the elbow play crucial roles in maintaining a stable and congruent joint throughout a range of motion and during periods of applied stress. The primary ligamentous complexes are the ulnar (or medial) collateral ligament (UCL) and the lateral (or radial) collateral ligament (LCL) of the elbow. As noted, injury to the LCL is often seen as a component of the “terrible triad of the elbow” and is repaired at the time of fixation of radial head and coronoid injuries. The UCL is located on the medial elbow and has three bands (oblique, posterior, and anterior) with the primary anterior band originating from the medial humeral epicondyle and inserting on the proximal ulna. This portion of the UCL provides primary stability to the elbow when under valgus stress. Injury to the UCL is commonly seen in throwing athletes, particularly in competitive baseball. The diagnosis of UCL injury is made from clinical history, physical exam, and imaging (often both plain radiographs and MRI). A trial of nonoperative management is often used for partial injuries and those occurring in younger athletes. This involves rest from throwing, anti-inflammatories, physical therapy, and a graduated return to sport [35]. Most acute and complete injuries are treated operatively, especially in high-level athletes. The first described surgery for UCL reconstruction was performed on major league pitcher Tommy John and thus has become known as “Tommy John surgery.” Rather than repairing the torn or damaged ligament, reconstruction with an expendable autograft tendon (e.g., the palmaris longus) or allograft tendon is the preferred treatment of

choice. The results of the surgery have been favorable with over 80% of throwers returning to their previous level of sport [36].

26.5.2 Distal Biceps Rupture

The biceps courses from the shoulder through the arm's anterior compartment and across the elbow to insert on the radial tuberosity. The radial tuberosity is located on the ulnar side of the proximal radius. The biceps muscle functions as the strongest forearm supinator and assists in elbow flexion. Injury to the biceps most commonly occurs at its origin, specifically the origin of the long head of the biceps on the superior glenoid [37]. Rupture at this level can cause the classic "Popeye" deformity, representing a cosmetic loss of normal biceps contour. Rupture of the biceps at its distal insertion is less common. Distal biceps ruptures are most common in male patients aged 40–50 and are thought to occur from excessive eccentric loading of the elbow as it is brought from flexion to extension [38]. These can include both acute and chronic injuries as well as partial- or full-thickness tears. Patients will typically report a "pop" followed by pain during heavy lifting. In addition to swelling, ecchymosis, and weakness, a classic exam maneuver is the "hook test" in which the examiner attempts to "hook" the biceps tendon at the elbow. If unable to do so, the test provides excellent sensitivity and specificity for diagnosis of a distal biceps rupture [39]. A "Popeye" type deformity can also be seen in these patients as the contour of the biceps muscle is shifted proximally after rupture. Management of distal biceps ruptures is typically surgical repair. Nonsurgical management is reserved for lower-demand patients and will most often result in a painless elbow but with some weakness in activities involving forearm supination [40]. It is preferable to perform surgical repair within 1–2 weeks of the injury to prevent significant proximal retraction of the ruptured tendon into the arm. The goal of repair is to securely re-anchor the biceps tendon to the radial tuberosity. Many surgical techniques exist and include various configurations of suture anchors or interference screws to secure the tendon [38]. Overall good functional outcomes are seen following repair with typically near full return of pre-injury strength and motion. Complications following surgery vary based on technique but can include injury to the lateral antebrachial cutaneous nerve, re-rupture, and heterotopic ossification [41].

26.6 Arthritis

26.6.1 Elbow Arthritis

Elbow arthritis is relatively uncommon and affects less than 2% of the population [42]. As with other arthritic joints, primary patient complaints include pain and loss of motion. Arthritis in the elbow is most commonly secondary to rheumatoid arthritis or posttraumatic causes. Other causes include primary arthritis, hemophilic arthropathy, and crystalline arthropathy. The diagnosis is made through a clinical history, physical exam, and typically plain radiographs. Radiographs demonstrate the usual arthritic findings of joint space narrowing, osteophytosis, and subchondral sclerosis (Fig. 26.8). Initial management includes activity modification, nonsteroidal anti-inflammatory medications, corticosteroid injection, bracing, and therapy. For patients with rheumatoid arthritis, nonoperative management is increasingly successful due to the advent and increasing use of disease-modifying antirheumatic drugs (DMARDS) to limit disease progression [43]. For patients that have significant symptoms despite nonoperative measures, surgical options exist. Initial surgical strategies for an arthritic elbow may vary somewhat from other joints with end-stage arthritis. In patients primarily limited by decreased motion, surgical removal of osteophytes and release of soft tissue contractures can be of benefit (Fig. 26.8a) [44]. This can be done through both open and arthroscopic surgical approaches. For patients with severe arthritis and pain, total elbow arthroplasty (replacement) is an option. There are multiple implant designs, but the most common is a semi-constrained prosthesis which functions as a "sloppy hinge" [45]. The proximal

Fig. 26.8 Elbow arthritis. (**a**) Lateral radiograph demonstrating exuberant osteophytes surrounding the elbow. Patient was treated with debridement of the posterior and anterior osteophytes with improved range of motion after surgery. (**b**) AP and (**c**) lateral radiographs demonstrating severe rheumatoid arthritis with near fusion of the elbow joint. This elbow was treated with total elbow arthroplasty. (**d**) AP and (**e**) lateral radiographs of cemented and semi-constrained total elbow arthroplasty

portion of the implant is secured in the humeral canal, and the distal portion is fixed within the proximal ulna (Fig. 26.8d, e). Unlike shoulder, hip, or knee replacements, elbow replacements carry fairly cumbersome activity restrictions such as the lifetime recommendation to not lift over 5 pounds in the operative arm. Despite this, elbow arthroplasty has proven to provide improved function and pain relief in the appropriate patients. Some of the best results are seen in rheumatoid arthritis patients and elderly patients with low functional demands [46]. Complications include infection, implant loosening and failure, wound complications, and periprosthetic fracture [47]. Though elbow arthritis can be difficult to treat, both nonsurgical and surgical measures can be of benefit in restoring motion and relieving pain.

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Common Clinical Conditions of the Hand and Wrist

27

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Contents

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Goals and Objectives

- *Goals*: To familiarize the readers with the more common hand and wrist conditions of the musculoskeletal system to give them an understanding of the epidemiology, presentation physical exam, physical exam, work-up, treatment, and possible complications of these conditions.
- *Objectives*: At the conclusion of the chapter, the learner should be able to understand the presentation, physical exam, initial evaluation, and treatment options of the following conditions: basilar thumb arthritis, flexor tendon injuries, hand infections, trigger fingers, Dupuytren's disease, scaphoid fractures and nonunions, scapholunate ligament injuries, distal radius fractures, carpal tunnel syndrome, DeQuervain's tenosynovitis, and ganglion cysts

27.1 Basilar Thumb Arthritis

Background: Basilar thumb arthritis is arthritis found at the thumb carpometacarpal (CMC) joint. This is the second most common location for hand arthritis behind distal interphalangeal joint arthritis. It is more common in women than men with up to sixfold increase in incidence. It has also been shown to be more common in Caucasians than in Native Americans, Asians, or African Americans. It also increased in prevalence with increasing age with studies showing 6.6% of individuals 40–49 years old with radiographic evidence of thumb CMC arthritis and 36.4% in individuals over 80 years of age [1]. Radiographic findings do not always correlate with patients' symptoms, but when symptomatic it can cause up to 50% impairment to that extremity [2].

27.1.1 Anatomy and Pathophysiology

The thumb CMC joint is made up of the trapezium and the thumb metacarpal. The trapezium has a saddle-shaped distal joint surface that allows for a high degree of motion in multiple planes. Due to the mobility of this joint, soft tissue stabilizers are of utmost importance to maintain position and function of the joint. Historically it has been thought that the deep anterior oblique ligament ("beak ligament") was the pivot point around which the thumb rotated and that attenuation of this ligament leads to progression of the disease. More recently, the dorsal ligament complex of the trapeziometacarpal joint has been shown to be of substantial importance for joint stabilization [3].

27.1.2 Presentation Physical Exam

Patients will typically present with pain and swelling of the base of the thumb with specific activities including pinching and grasping. The

CMC grind test is performed by exerting an axial load across the thumb CMC with concomitant circumduction [4]. A positive test will reproduce the pain the patient experiences with their normal activities. Pinch strength can also be compared to the contralateral side as it has been recently shown that a decrease in pinch strength can be present even before radiographic changes are evident.

27.1.3 Imaging

Plain radiographs are the study of choice to evaluate basilar thumb arthritis (Fig. 27.1). This should consist of three view radiographs including an AP, lateral, and oblique view of the hand or wrist. Specialized radiographic views (Betts or Roberson) visualize the trapeziometacarpal joint in profile and allow for evaluation of disease severity. The Eaton-Littler staging system is widely used to stage basilar arthritis and is based on radiographic criteria [5].

27.1.4 Eaton-Littler Classification

Stage I	Subtle carpometacarpal joint space widening
Stage II	Slight carpometacarpal joint space narrowing, sclerosis, and cystic changes with osteophytes or loose bodies <2 mm
Stage III	Advanced carpometacarpal joint space narrowing, sclerosis, and cystic changes with osteophytes or loose bodies >2 mm
Stage IV	Arthritic changes in the carpometacarpal joint as in Stage III with scaphotrapeziotrapezoid (STT) arthritis

27.1.5 Treatment

Nonsurgical interventions are the first-line treatment for mild symptoms. Hand exercise programs, heat, joint protection education, and hand orthoses can be beneficial in symptomatic treatment of early thumb CMC arthritis. Additionally, oral and topical NSAIDs have good short- and medium-term symptomatic relief for this condition [6]. Corticosteroid injection into the thumb CMC joint is another viable non-operative treat-

Fig. 27.1 Radiograph of severe basilar thumb arthritis

ment option. A recent systematic review found that corticosteroid injections can offer good symptomatic relief in patients with mild disease up to 1 year [7].

Surgical treatment is discussed after the patient has failed a trial of non-operative intervention. Joint-preserving operations may be reasonable for patients with early-stage arthritis. This may include arthroscopic debridement and possible capsulorrhaphy or a first metacarpal dorsal closing wedge extension osteotomy [8]. For more advanced disease, stage II–IV, joint-altering procedures must be considered. This may include a complete trapeziectomy or trapeziectomy with ligament reconstruction with tendon interposition (LRTI). Another option for young laborers with stage II–III disease is a trapeziometacarpal arthrodesis as it may preserve grip strength, though it is associated with a higher complication rate than trapeziectomy procedures [9]. The possible use of silicone or metallic implants has been investigated and is currently not recommended due to their high rate of failure or dislocation of these devices.

27.1.6 Complications

The main risk of non-operative interventions includes inadequate symptomatic relief. Specifically for corticosteroid injections, there is a risk of adverse reactions including skin irritation, infection, and overlying skin hypopigmentation. For surgical intervention for basilar thumb arthritis, there is a risk of metacarpal subsidence or interposition failure [9].

27.2 Flexor Tendon Injuries

Background: Flexor tendon injuries are relatively rare injuries with an incidence of 4.83 per 100,000 people [10]. These injuries are typically due to volar lacerations, so they may present with concomitant neurovascular injuries. The severity of the injury and overall prognosis are related to the level at which the tendon is injured.

27.2.1 Anatomy and Pathophysiology

There are several flexor muscles that aid in finger and wrist motion which include the flexor digitorum profundus and superficialis, flexor pollicis longus and brevis, and flexor carpi radialis and ulnaris. There are two separate blood supply systems for the tendons. One is through diffusion through the synovial sheath. There is also direct blood supply to the other tendons that are outside of a synovial sheath. This includes the small blood vessels that are within the vincula that connect the FDS and FDP to the bone.

27.2.2 Presentation Physical Exam

The majority of patients present with a laceration over the volar aspect of the finger, hand, wrist, or forearm. The main presenting symptom will be loss of active flexion strength of the involved digit. A thorough exam of the distal aspect of the extremity is key to determine exactly which tendons are involved as well as if there is concomitant neurovascular injury. During the physical exam, each joint should be isolated to assess for the ability to actively flex and extend at that joint specifically.

27.2.3 Imaging

Radiographs are obtained to evaluate if there is any concomitant bony injury that should also be addressed. Advanced imaging is not routinely obtained as further evaluation of associated neurovascular injuries can typically be elucidated with physical exam and further explored at the time of surgery.

27.2.4 Classification

Zone of Flexor Tendon Injury (Fig. 27.2) [11]

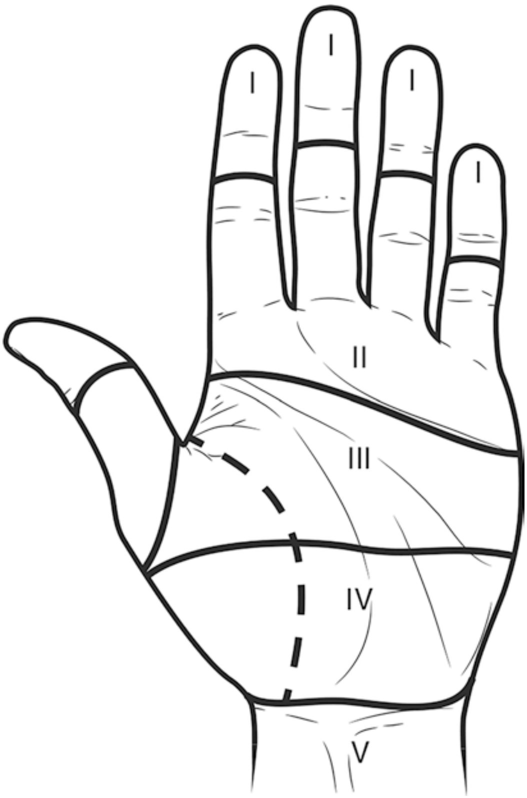

Fig. 27.2 Illustration of the palmar view of the hand demonstrating the anatomically based classification of flexor tendon injuries [71]

Zone I	From the FDS insertion to the FDP insertion
Zone II	From the proximal aspect of the A1 pulley to the FDS insertion
Zone III	From the distal aspect of the transverse carpal ligament to the A1 pulley
Zone IV	The carpal tunnel
Zone V	From the proximal border of the transverse carpal ligament to the musculotendinous junction in the forearm

27.2.5 Treatment

An acute laceration that involves over 60% of the tendon should be repaired primarily [12]. This may include multiple core suture and epitendinous suture configurations (Fig. 27.3). Chronic injuries are typically treated with staged tendon reconstruction [13].

27.2.6 Complications

The most common complication after flexor tendon repair is adhesion formation and decreased range of motion. There has also been found a 15–25% risk of rerupture of the previously repaired tendons [14]. Zone II lacerations are especially prone to complications, due to their reliance on predominately indirect nutritional supply through synovial diffusion. It is also possible to create a trigger finger due to the increased bulk of the tendon at the repair site that has to pass through the same-size fibro-osseous tunnel [14].

27.3 Infection

27.3.1 Background

Finger and hand infections are a common complaint to orthopedic surgeons and the emergency department. The complex anatomy of the hand makes it susceptible to unique infections.

27.3.2 Anatomy and Pathophysiology

Staphylococcus aureus has been implicated in 80% of all hand infections [15]. The next most common organisms include *Streptococcus* spp. and Gram-negative organisms. It has also been found that MRSA infections have been increasing over the last decade and are now implicated in up to 78% of all hand infections [16].

27.3.3 Presentation Physical Exam

The patient will typically report a recent injury to the area that was the cause of local inoculation, but it is also possible to have hematogenous seeding. The affected digit or location of infection will be swollen, erythematous, and tender to palpation. The examiner may be able to palpate underlying fluctuance, or there may be frank

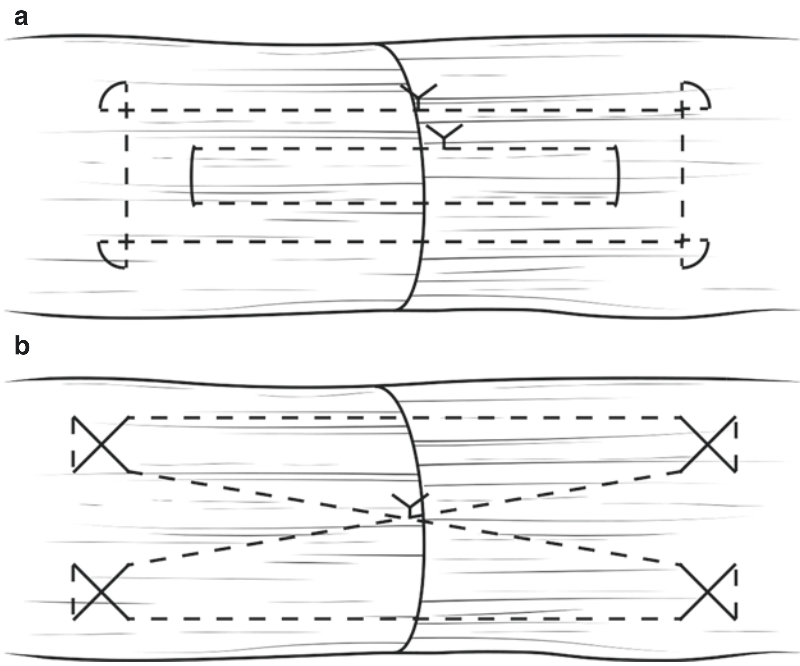

Fig. 27.3 An example of two suture fixation techniques with four core suture strands: a horizontal mattress suture added to Kessler's technique (**a**) and the cross-locked cruciate technique (**b**) [71]

purulence draining from the initial site of injury. Infection labs including WBC, ESR, and CRP may be non-specifically elevated in the setting of an acute infection with or without fever.

27.3.4 Imaging

Many of these infections can be diagnosed and treated without the need for advanced imaging. If there is doubt as to the presence of an abscess in association with overlying cellulitis or to determine the full extent of an infection in a deeper space, then an ultrasound or MRI for further characterization may be obtained.

27.3.5 Classification

Paronychia is an infection beneath the eponychial fold and is associated with manicures, fingernail biting, and hangnails. With acute infection an abscess will form in this area. If not treated expeditiously, then it may spread beneath the nail plate itself. These may be treated with a digital block and decompression of the abscess. If it has spread beneath the nail plate, then the nail should also be removed. The patient should then be discharged with local wound care instructions and antibiotics.

Felon is a closed-space infection of the finger pulp. This can cause exquisite pain as it acts like acute compartment syndrome within the pulp due to increased pressure in the many septations within this area. This should also be treated with a digital block, decompression, antibiotics, and local wound care.

Pyogenic flexor tenosynovitis is a bacterial infection within the flexor tendon sheath. Clinical diagnosis is aided with the use of Kanavel's four cardinal signs which include exquisite tenderness over the course of the sheath, limited to the sheath; resting semiflexed position of the finger; exquisite pain with passive extension of the finger; and symmetrical or fusiform swelling of the entire finger [17]. If the patient presents with less than 24 h of symptoms, then an initial trial of IV antibiotic treatment and strict elevation may be attempted. The gold standard for treatment is urgent irrigation and debridement of the flexor tendon sheath (Fig. 27.4) followed by IV antibiotics and wound care [18].

Deep-space infections of the hand can involve any of the deep spaces of the hand including the

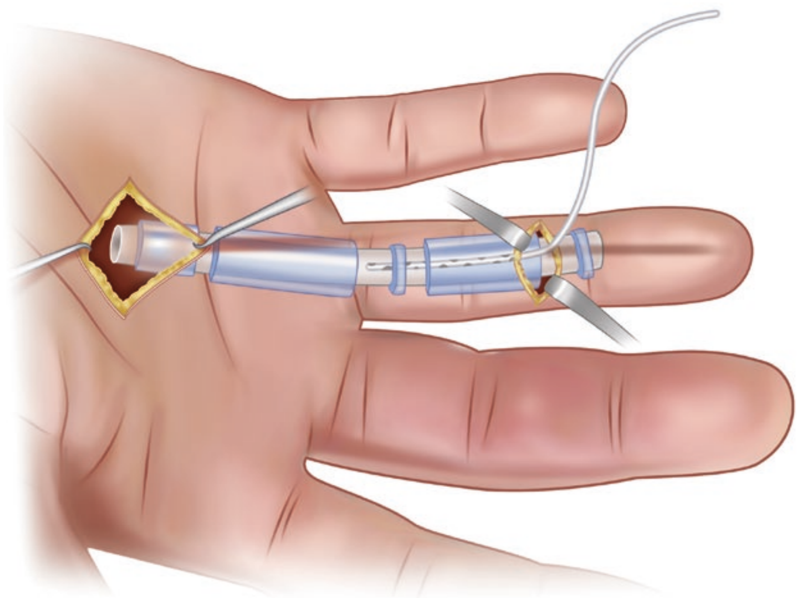

Fig. 27.4 Closed irrigation for treatment of pyogenic flexor tenosynovitis [18], illustrated in a retrograde direction here, but also may commonly be performed antegrade

thenar, hypothenar, dorsal subaponeurotic, midpalmar, and deep palmar spaces. It is also possible for these infections to spread to other spaces due to known communications between the areas. An MRI may aid in localization of the abscess, and definitive treatment includes incision and debridement in the operating room followed by appropriate antibiotic treatment.

Septic arthritis is infectious arthritis that may occur in any joint in the wrist, hand, or finger. These infections may have a rapid clinical course, and bacterial toxins, in combination with the patient's immune response, may create substantial damage to the articular cartilage. Exquisite pain with joint micromotion, sometimes coupled with joint fluid analysis from arthrocentesis, allows for diagnosis. Treatment involves irrigation and debridement of the joint followed by appropriate antibiotic treatment.

27.3.6 Treatment

General treatment guidelines consist of surgical decompression of the associated fluid collection, appropriate antibiotic treatment, and local wound care as previously discussed [19, 20].

27.3.7 Complications

If these infections are not treated appropriately, it can lead to long-standing complications including finger stiffness, loss of dexterity, or even loss of the digit. If allowed to progress, it may also lead to systemic involvement and sepsis.

27.4 Trigger Finger

27.4.1 Background

Trigger finger is most common in the fifth to sixth decades of life. It is six times more common in women than in men. The lifetime risk of developing trigger finger is 2–3% in the general population [21]. This increases to almost 10% in diabetics [22].

27.4.2 Anatomy and Pathophysiology

Trigger finger is known as tendovaginitis as it is due to pathologic inflammatory changes of the retinacular sheath (tendovagina). The retinacular

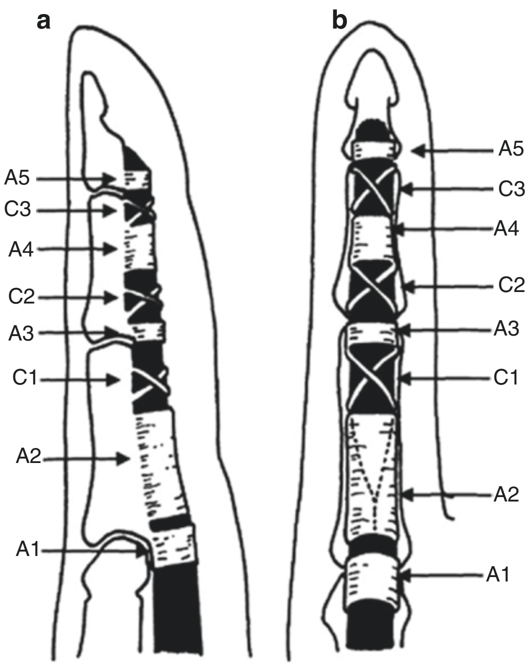

Fig. 27.5 Anatomy of flexor pulley system [73]

sheath forms a pulley system along each digit that maximizes the flexor tendon force as well as prevents bowstringing of the tendons. The most commonly involved pulley is the first annular pulley (A1), which is found at the level of the metacarpal head on the volar surface (Fig. 27.5). These inflammatory changes are due to various factors including repetitive finger movements and local trauma. This will result in increased friction at the level of the pulley and cause difficulty with flexor tendon gliding [21].

27.4.3 Presentation Physical Exam

Patients may initially present with a painless clicking with finger flexion and extension. This may then progress to a painful popping and catching. It can progress to locking of the digit in flexion or extension which may or may not be passively correctable. Physical exam will reveal tenderness over the A1 pulley, possibly with a palpable mass in the same location. One may also be able to reproduce the triggering of the finger with passive range of motion of the digit.

27.4.4 Imaging

Imaging is not routinely indicated for trigger finger.

27.4.5 Treatment

Initial treatment is with nonsurgical interventions. Activity modification, NSAIDs, and nighttime splint should be the first line of treatment. If there is no symptomatic improvement with these interventions, then a corticosteroid injection at the level of the A1 pulley should be considered. Success rates of injection vary, but the vast majority (93%) of patients obtain at least short-term relief, while long-term relief is also reported in 40–60% of individuals [23]. If the patient fails these treatments, then a surgical release of the A1 pulley should be performed. This may be percutaneous or open based upon the surgeon's preference [24].

27.4.6 Complications

Corticosteroid injections may result in dermal atrophy, overlying hypopigmentation of the skin, or in very rare cases flexor tendon rupture. With surgical release of the A1 pulley it is possible to injure the digital nerve or artery or to perform an incomplete release leading to recurrence [25].

27.5 Dupuytren's Disease

27.5.1 Background

Dupuytren's disease is a myeloproliferative disease that leads to flexion contractures of the hand. It has been found to have a genetic component and is inherited in an autosomal dominant pattern with variable penetrance. It is most common in the fifth to seventh decades of life, and it has been found to affect men more than women with a 2:1 ratio [26].

27.5.2 Anatomy and Pathophysiology

This disease is caused by the inhibition of the genes regulating the natural breakdown of collagen and the upregulation of the genes that promote structural development of collagen. The increased collagen formation can result in nodules and cords along the volar aspect of the hand. Myofibroblasts in the cords contract as the disease progresses and are responsible for generating contractures [27].

27.5.3 Presentation Physical Exam

Patients will present with palpable nodules or cords along the palmar surface of the hand that may resemble contracted flexor tendons (Fig. 27.6). The most commonly affected digit is the ring finger, but it may involve all of the digits to varying degrees. The contracture has been found to affect the metacarpal phalangeal joint prior to affecting the proximal interphalangeal joint. With progression of the disease, individuals will have difficulty opening the hand to grip objects and perform everyday tasks. When evaluating these patients, it is essential to record the range of motion of each digit at each joint in degrees [28].

Fig. 27.6 Clinical presentation of Dupuytren's contracture

27.5.4 Imaging

Imaging is not routinely indicated for Dupuytren's contracture.

27.5.5 Treatment

The presence of nodules or cords alone does not require treatment. Once contractures reach the point that they are inhibiting function, then treatment should be offered. Collagenase injection into the cord with manipulation is a minimally invasive technique that has very promising results with good improvement in range of motion [29]. Another option is percutaneous needle aponeurotomy, in which a needle is used with multiple passes to section the contracted cord followed by early active and passive range-of-motion exercises. Surgery is reserved for recalcitrant cases that failed other treatment or severe cases that are not amenable to less invasive techniques. This involves open fascial excision of the involved areas [30, 31].

27.5.6 Complications

Collagenase injection with manipulation has been associated with local ecchymosis and swelling. There is also a risk of skin tears if there is overaggressive manipulation. Percutaneous aponeurotomy has a risk of digital artery or nerve injury. Open fascial excision places the patient at risk for wound healing complications and infections. No matter what the treatment method is, recurrence is likely between 3 and 10 years following treatment [31].

27.6 Wrist

27.6.1 Scaphoid Fracture and Nonunion

Background: The scaphoid is injured in approximately 15% of all acute wrist injuries. It also accounts for 60% of all carpal fractures making it the most commonly injured carpal bone. It is most commonly injured in men aged 15–40 years old [32].

27.6.1.1 Anatomy and Pathophysiology

The scaphoid is described as having a proximal and distal pole with the waist delineating the two. It is a unique bone in that 80% of the scaphoid is covered with articular cartilage, limiting areas of vascular inflow. This tenuous blood supply is what confers the risk of poor outcomes to scaphoid fractures. The dorsal scaphoid artery is a branch of the radial artery, enters at the level of the scaphoid waist, and supplies the proximal 70–80% of the scaphoid. The volar scaphoid artery is either a branch of the radial artery or the superficial palmar arch, enters at the distal tubercle, and supplies the distal 20–30% of the scaphoid. This means that the proximal pole of the scaphoid depends solely on intra-osseous blood flow for perfusion [33].

27.6.1.2 Presentation Physical Exam

The patient typically presents following a fall onto a hyperextended and radially deviated wrist. They will have pain and swelling over the radial aspect of the wrist. Patients with a scaphoid injury will typically have tenderness dorsally at the anatomic snuffbox as well as volarly over the scaphoid tubercle. Elicited pain with resisted pronation is also common. This is typically in conjunction with reduced grip strength and possible pain with thumb range of motion [34].

27.6.1.3 Imaging

Initial imaging should include wrist radiographs including AP, lateral, 45 degree pronated oblique, and scaphoid view, which is 30 degrees of wrist extension and 20 degrees of ulnar deviation.

Fig. 27.7 Displaced scaphoid waist fracture

Fractures may be difficult to visualize on radiographs. If there is a high clinical suspicion for scaphoid fracture but negative radiographs, one may pursue advanced imaging or immobilize the patient with a thumb spica and repeat imaging in 10–14 days [35]. An MRI of the wrist may also be used to diagnose acute occult fractures with 90–100% sensitivity and 90% specificity [36]. If there is a fracture identified on plain radiograph, then one must determine if it is displaced or non-displaced as this has implications on treatment options (Fig. 27.7). If one is unable to determine if there is displacement on plain radiograph, then a CT scan would be the imaging modality of choice.

27.6.1.4 Treatment

Stable, non-displaced, acute fractures can be treated with cast immobilization for 10–12 weeks with a thumb spica cast. The healing rate of non-displaced scaphoid waist fractures treated with cast immobilization is 88–95% if treatment was initiated within 3 weeks of injury. Athletes and those patients that wish to return to activity in a more expedited manner may wish to discuss the possibility of surgical fixation as this may allow them to return to activity as early as 6 weeks from the time of surgery [37].

Unstable, displaced, acute fractures as well as proximal pole fractures should be treated with surgery as they have a higher risk of nonunion and avascular necrosis. As the scaphoid is 80% covered with articular cartilage, it is most common to use a headless compression screw for fixation that can be recessed below the margin of the articular cartilage. It has been found that a 95% union rate can be achieved with either the dorsal or volar approach as long as there is appropriate screw position, which is defined as within the central one third of the scaphoid [38].

27.6.1.5 Complications

Complications of cast immobilization include potential skin breakdown, increased time to union, and stiffness of the immobilized joints. In non-displaced fractures treated with cast immobilization, the rate of nonunion can be as high as 5–10%. It has also been found that there is up to 10% rate of nonunion in displaced scaphoid fractures that were treated surgically. Nonunion of the scaphoid can result in chronic pain and decreased grip strength, but it can also lead to a condition known as scaphoid nonunion advanced collapse (SNAC) which is progressive wrist arthritis due to altered mechanics [39–40].

27.6.2 Scapholunate Ligament Injury

27.6.2.1 Background

Scapholunate (SL) ligament injuries occur acutely in up to 54.5% of intra-articular distal radius fractures or carpal fractures. SL ligament injuries may also present as a degenerative tear and have been found to be present in over 50% of the population over the age of 80 years old [41].

27.6.2.2 Anatomy and Pathophysiology

The SL ligament has three components that connect the scaphoid and lunate. These include the volar, dorsal, and proximal components. These three components combine to create a C-shaped ligament. The majority of the strength of the ligament is conferred by the dorsal component. The bones of the proximal carpal row have no muscular attachments but rather are connected to each other through bony articulations and complex ligamentous structures. In an uninjured wrist, the motion of the proximal row reflects the global motion of the wrist. At baseline the scaphoid has a tendency towards flexion and the triquetrum a tendency towards extension with the lunate held in balance in-between the ligamentous structures. If there is disruption of the SL ligament, the scaphoid will collapse into flexion, and the lunate will go with the triquetrum into extension. This will result in abnormal motion and the development of degenerative changes at the radial styloid and scaphoid [42].

27.6.2.3 Presentation Physical Exam

A patient with an acute tear typically presents after a fall onto an outstretched hand with the wrist in extension, ulnar deviation, and midcarpal supination. This will cause the capitate to drive into the scapholunate articulation and result in a tear of the SL ligament [43]. These patients will present with acute wrist pain that is most significant over the dorsal radial aspect of the wrist. Pain can be elicited with loading of the wrist in a push-up position. There is also an associated decreased grip strength and range of motion of the wrist. A patient with a chronic tear will more likely present with a slow onset of persistent wrist pain in the same distribution without specific inciting event. The Watson scaphoid shift test assesses for anomalous scaphoid motion. The arm is held in a small amount of pronation, and the examiner applies a dorsal force over the scaphoid while passively moving the wrist from ulnar deviation and extension to radial deviation and flexion. If there is an injury to the SL ligament, the scaphoid will subluxate onto the dorsal rim of the distal radius, and when the force is removed the scaphoid will relocate with a clunk back into the scaphoid fossa of the distal radius. This relocation should reproduce the patient's pain.

27.6.2.4 Imaging

Initial imaging should include plain radiographs with AP, lateral, scaphoid, and bilateral PA clenched pencil views. On the AP view, one can

Fig. 27.8 AP wrist radiograph with scapolunate ligament disruption with associated radial styloid fracture

evaluate for SL interval widening, which, if present, represents a complete tear of the SL ligament. One can also evaluate scaphoid height as well as the ring sign, indicative of scaphoid flexion. The bilateral pencil grip view puts stress across the SL ligament and will show dynamic instability, which can be indicative of a partial tear or a complete tear with intact secondary stabilizers. A SL gap over 3 mm on this view is positive for a SL ligament injury [44] (Fig. 27.8). Arthrography can also be completed under fluoroscopy to evaluate for contrast communication between the radiocarpal and midcarpal compartments. MRI and MRA can also be obtained to evaluate the continuity of the ligament. Despite this, wrist arthroscopy remains the gold standard for diagnosis of acute and chronic SL ligament injuries as it can diagnose, grade, and possibly treat the injury.

27.6.2.5 Treatment

Initial treatment with immobilization is typically not recommended as it cannot reduce the scapholunate gap nor has it been shown to provide symptomatic relief in the literature. Primary repair of the ligament in the acute setting can result in good pain relief and return to activity, but it has been shown to have only fair to poor outcomes if performed in subacute or chronic injuries. Arthroscopic debridement with k-wire fixation of the scaphoid and lunate provides reliable pain relief in the setting of a partial tear. There may also be a role for the addition of capsular shrinkage with the arthroscopic procedure to enhance stability again only in a partial tear of the SL ligament [45]. With complete tears of the SL ligament as well as subacute and chronic partial tears, the recommendation is ligament reconstructive procedures [46].

27.6.2.6 Complications

It is unknown exactly what percent of patients that sustain an acute scapholunate ligament disruption will progress to scapholunate advanced collapse (SLAC) wrist [47]. The scaphoid flexion and lunate extension cause abnormal distribution of forces across the midcarpal and radiocarpal joints. This will result in progressive arthritis in these areas.

27.6.3 Distal Radius Fractures

27.6.3.1 Background

Distal radius fractures are one of the most common fractures in adults making up approximately 18% of all fractures sustained in this group, resulting in over 640,000 per year. They are more common in women than in men with approximately 32% of all fractures seen in women over the age of 35 being distal radius fractures. In 2007 Medicare paid over $170 million for distal radius fracture-related care [48].

27.6.3.2 Anatomy and Pathophysiology

The distal radius articulates with the proximal carpal row. It also articulates with the distal aspect of the ulna creating the distal radioulnar joint (DRUJ). Injuries to the distal radius can also result in injuries of the carpus or DRUJ and should also be evaluated.

27.6.3.3 Presentation Physical Exam

Injuries to the distal radius are typically sustained by a fall onto an outstretched hand as the force will be transmitted from the carpus to the distal radius. The patient will typically present with swelling and visible deformity of the wrist and pain and palpable crepitus at the level of deformity. It is important to also evaluate the entirety of the ipsilateral extremity for concomitant fractures. It is also important to perform a detailed neurovascular exam as distal radius fractures do confer a risk of developing acute carpal tunnel syndrome. Acute carpal tunnel syndrome has been found to occur in 5.4% of surgically treated distal radius fractures [49].

27.6.3.4 Imaging

Initial evaluation should include plain radiographs of the wrist (Fig. 27.9). These radiographs are used to assess if there is intra-articular involvement as well as overall alignment of the fracture. The important components include radial height, radial inclination, and volar tilt. These features will impact the final treatment of the fracture. Complex fractures with intra-articular fragmentation may benefit from a CT scan to aid in surgical planning [50].

27.6.3.5 Classification

There are several classification systems for distal radius fractures, but none of them are ubiquitous. There are several well-known eponymous distal radius fractures. Colles' fractures are low-energy extra-articular fractures that are dorsally displaced. Smith's fractures and Colles' fractures are similar as they are also low-energy and extra-articular, but they are volarly displaced. Chauffer's fractures are radial styloid fractures. Barton's fractures are intra-articular fractures involving the volar lip of the distal radius that result in a fracture dislocation of the radiocarpal joint.

27.6.3.6 Treatment

When deciding between operative and non-operative treatment of distal radius fractures, it is important to consider the age and activity level of the patient, whether it is the dominant or non-dominant arm, if there is articular involvement, and the overall alignment of the fracture. Surgical intervention is indicated in those patients with radial shortening >3 mm, dorsal tilt >10 degrees, or intra-articular step-off >2 mm measured on post-reduction radiographs. If the fracture does not meet these criteria, then it can be most likely successfully treated with cast immobilization. It has been proposed for individuals over the age of 65 to be treated with casting instead of surgical fixation, but the current guidelines recommend not using a hard age cut-off but rather factoring that in with activity level, bone quality, and involvement of dominant extremity. Surgical intervention can be accomplished with volar locking plate technology, fragment specific fixation, dorsal bridge plate fixation, or external fixation with or without percutaneous Kirschner wire fixation for augmentation [51–52].

27.6.3.7 Complications

Distal radius fractures can result in acute carpal tunnel syndrome. This is a surgical emergency and requires immediate carpal tunnel release. Prospective studies have found that approximately 90% of young adults will develop radiocarpal arthritis if there is an intra-articular step-off >2 mm that is not corrected, which is why surgical intervention is typically advocated in this group [53]. As with any fracture, malunion or nonunion is possible. One unique complication found in non-displaced distal radius fractures that are treated non-operatively includes extensor pollicis longus rupture caused by local attrition from impingement or local ischemia of the tendon at the level of the fracture due to swelling within the extensor tendon sheath.

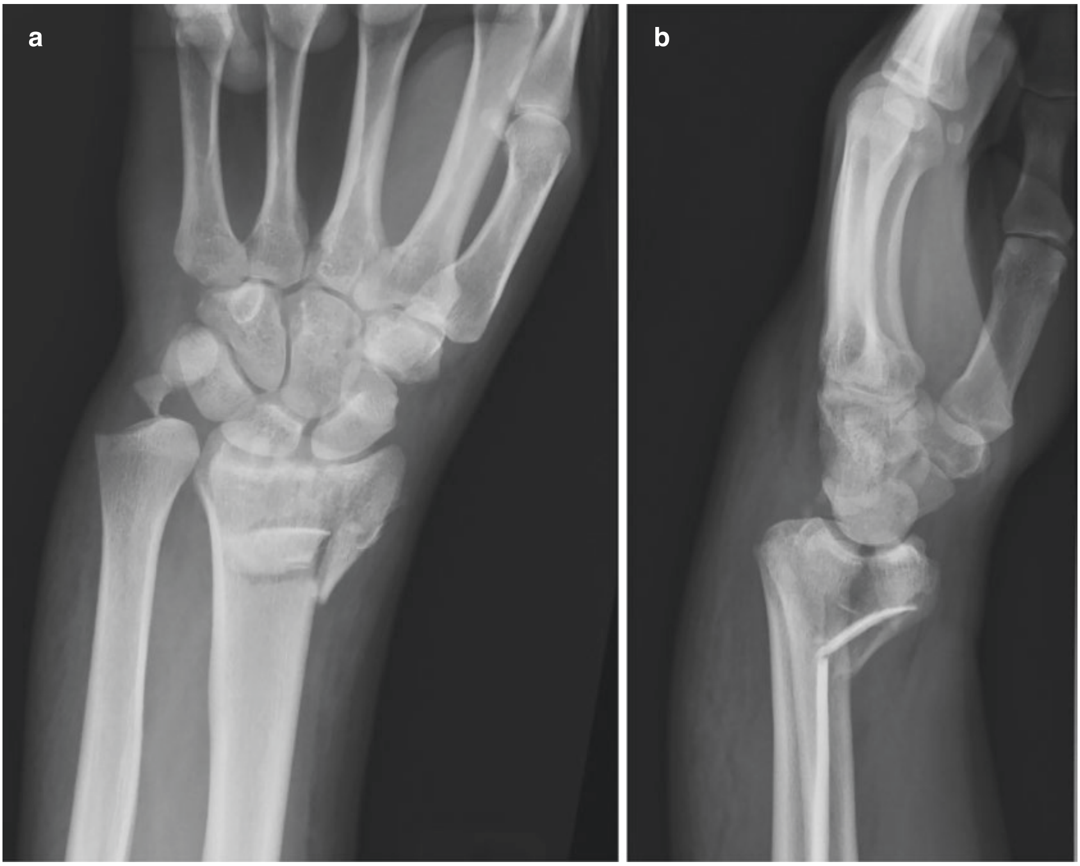

Fig. 27.9 AP (**a**) and lateral (**b**) views of distal radius fracture

27.6.4 Carpal Tunnel Syndrome

27.6.4.1 Background

Carpal tunnel syndrome refers to compression neuropathy of the median nerve as it courses through the carpal tunnel at the wrist. It is a very common problem affecting between 0.1% and 10% of the general population. As of 2007, it also accounts for approximately 500,000 surgical cases per year, which when considering cost of treatment and time out of work has an economic impact of approximately $2 billion annually [54].

27.6.4.2 Anatomy and Pathophysiology

The borders of the carpal tunnel include the scaphoid tubercle and trapezium radially, hook of hamate and pisiform ulnarly, the proximal carpal row dorsally, and the transverse carpal ligament (TCL) volarly. The carpal tunnel contains the tendons of the flexor pollicis longus (FPL), four tendons of the flexor digitorum profundus (FDP), four tendons of the flexor digitorum superficialis (FDS), and the median nerve. The FPL is the most radial structure, and the median nerve is the most superficial structure. The cause of carpal tunnel syndrome is compression of the median nerve within the carpal tunnel. This increase in pressure within the tunnel can be due to inflammation from repetitive motion in previously normal underlying anatomy or in individuals with space-occupying lesions [55].

27.6.4.3 Presentation Physical Exam

Compression of the median nerve within the carpal tunnel presents with several classic findings including numbness and tingling in the thumb, index, long, and radial ring fingers, pain and par-

esthesias that wake the patient up at night, and clumsiness of the hand. These symptoms typically are more prevalent at night, and shaking of the hand may alleviate these symptoms. With a more prolonged course of nerve compression, the patient may also present with grip and pinch weakness due to thenar muscular atrophy. Identifying and diagnosing carpal tunnel syndrome relies heavily upon the physical exam. Specific physical exam tests aim to increase the pressure within the carpal tunnel causing further compression of the median nerve to reproduce the classic symptoms of carpal tunnel syndrome. Tinel's sign is percussion over the median nerve at the wrist and palm that if positive produces an electric shock sensation in the median nerve distribution. Phalen's test is flexing the wrist by gravity for 60 seconds. This is positive if it elicits numbness or tingling in the median nerve distribution. Durkan's median nerve compression test is manual pressure over the carpal tunnel for 30 seconds that will produce numbness or tingling in the median nerve distribution if positive [56]. It is also important to perform sensory testing using both innervation density measurements with static or dynamic 2-point discrimination as well as threshold sensory assessment using Semmes-Weinstein monofilament testing. It has been found that threshold sensory testing is more sensitive than density testing [57].

27.6.4.4 Imaging

Imaging is not typically indicated in the diagnosis of carpal tunnel syndrome. Electrodiagnostic studies that include nerve conduction studies in conjunction with electromyography are valuable for the diagnosis of carpal tunnel syndrome as well as a baseline for comparison during the patient's course of symptom evolution or treatment [58].

27.6.4.5 Classification

There is no specific classification of carpal tunnel syndrome other than the acuity of onset. Acute carpal tunnel syndrome is a syndrome comprised of acute onset of symptoms with rapid progression. Chronic carpal tunnel syndrome is a slow-onset syndrome with progressively worsening symptoms that typically begin with night symptoms and positional symptoms that progress to more pervasive symptoms.

27.6.4.6 Treatment

Acute carpal tunnel syndrome is a surgical emergency, and these patients should be taken immediately for carpal tunnel release using an open, mini-open, or endoscopic surgical technique depending upon surgeon preference. Chronic carpal tunnel syndrome is managed electively and may be amendable to nonsurgical interventions. Initial treatment may consist of night-time neutral wrist immobilization, which lessens pressure in the carpal tunnel. Ergonomic changes at work and home may also lessen exacerbation of symptoms [59]. Oral medications including NSAIDs, physical therapy, and soft-tissue gliding exercises have been found to have no impact on symptoms and are therefore not recommended. Corticosteroid injections into the carpal tunnel may be diagnostic as well as therapeutic for carpal tunnel syndrome. Following injection, approximately 76% of patients will have symptomatic relief for 6 weeks, but only 30% of patients will remain symptom-free one year after injection [60]. Diabetics have a decreased likelihood of symptomatic improvement after injection. The definitive treatment for carpal tunnel syndrome is surgical release of the transverse carpal ligament. This may be done with open, mini-open, or endoscopic surgical technique based upon the surgeon's preference [61].

27.6.4.7 Complications

Chronic severe carpal tunnel syndrome can result in permanent median nerve damage, which can result in persistent numbness, tingling, and decreased pinch and grip strength. In patients with severe carpal tunnel syndrome, approximately 20% of these individuals will have persistent symptoms even after surgical release [61].

27.6.5 De Quervain's Tenosynovitis

27.6.5.1 Background

De Quervain's tenosynovitis is tenosynovitis of the tendons of the first dorsal extensor compartment of the wrist, which includes the abductor

pollicis longus (APL) and the extensor pollicis brevis (EPB). De Quervain's tenosynovitis affects approximately 1.3% of all women and 0.5% of all men. It is more common in the dominant extremity, and it may be correlated with repetitive activities, which have been implicated as risk factors, including lifting and typing. It is most common in middle-aged individuals, but it may also be found in acute and self-limiting fashion in pregnant and lactating women [62].

27.6.5.2 Anatomy and Pathophysiology

The first dorsal extensor compartment of the wrist is located over the radial styloid and contains the abductor pollicis longus and extensor pollicis brevis. Friction through the compartment will lead to swelling and thickening of the extensor retinaculum and tendon sheath. Thickening of the retinaculum and sheath will result in a narrowed fibro-osseous tunnel causing pain with resisted movement of the tendons through this tunnel. During pregnancy the pathophysiology is different as it is typically due to the increased volume state resulting in swelling of the tissues [63] (Fig. 27.10).

27.6.5.3 Presentation Physical Exam

The patient typically presents with a gradual onset of pain over the dorsal radial aspect of the wrist over the radial styloid. This pain is typically worsened with grasping and raising objects with the wrist. The classic physical exam test is the Finkelstein test, in which the examiner grasps the patient's thumb and then deviates the patient's hand and wrist ulnarly. Similarly, the Eichhoff maneuver is performed by quickly ulnarly deviating the patient's wrist while their thumb is clasped within their clenched fist.

27.6.5.4 Imaging

Imaging is not indicated in this disease as it is a clinical diagnosis. If one is attempting to differentiate De Quervain's from other causes of pain including basilar thumb arthritis, then plain radiographs should be obtained. Otherwise, a clinical exam alone is needed for diagnosis.

27.6.5.5 Treatment

Nonsurgical treatment is the first line of treatment for De Quervain's and may include rest, thumb spica splinting, NSAIDs, and possibly first dorsal compartment corticosteroid injection [64]. Corticosteroid injection into the first dorsal compartment has been shown to result in full relief in 83% of patients. If the patient fails nonsurgical treatment and has undergone two corticosteroid injections and 6 months of conservative treatment without symptomatic improvement, then surgical release of the first dorsal compartment retinaculum should be discussed [65].

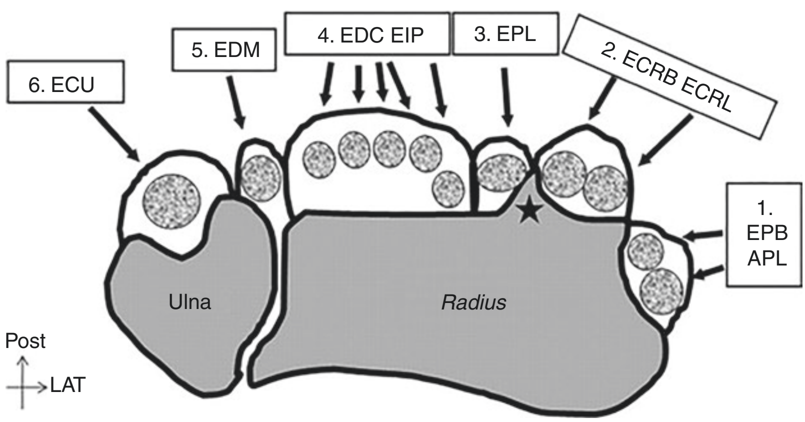

Fig. 27.10 Schematic of extensor tendons of the wrist in their six (1–6) separate compartments. *APL* abductor pollicis longus, *EPB* extensor pollicis brevis, *ECRL* extensor carpi radialis longus, *ECRB* extensor carpi radialis brevis, *EPL* extensor pollicis longus, *EIP* extensor indicis proprius, *EDC* extensor digitorum communis, *EDM* extensor digiti minimi, *ECU* extensor carpi ulnaris. ★ = Dorsal tubercle of the radius (Lister tubercule) [72]

27.6.5.6 Complications

Complications of corticosteroid injections have been previously discussed.

Care must be taken during surgical release to identify and protect the radial sensory nerve as it is in close proximity. Another risk of surgery is incomplete release resulting in persistent pain post-operatively, which may result from failure to identify and decompress tendons with multiple slips and septations within the sheath [66].

27.6.6 Ganglion Cysts

27.6.6.1 Background

Ganglion cysts are the most common soft tissue hand mass, representing approximately 70% of patients who present with a hand mass. They are benign soft tissue tumors that are treated based upon symptoms [67].

27.6.6.2 Anatomy and Pathophysiology

Approximately 70% of ganglion cysts are found dorsally originating from the scapholunate articulation. Other common sites of origin are from the volar aspect of the wrist at either the radiocarpal or scaphotrapeziotrapezoid joint (20%) and the flexor tendon sheath (10%). They are mucin-filled cysts that do not have a true synovial lining. It is thought that these cysts may actually be a herniation from the joint capsule or flexor sheath with fluid from those locations filling the cyst [67].

27.6.6.3 Presentation Physical Exam

On examination, the wrist ganglion is typically a firm rubbery feeling structure. It is typically not mobile as it is anchored in place by its stalk contiguous with the joint. The mass will transilluminate, which will differentiate it from other solid masses. Also, there is typically no associated erythema or warmth. People typically present for evaluation either due to pain, concern that the mass may be cancerous, or concern regarding cosmesis. Though over 80% of patients may report pain, less than 20% of these patients claim that the pain actually interferes with their activities of daily living.

Figure 27.11 shows the clinical presentation (a) and an intra-operative photograph (b) of distal wrist ganglion cyst.

27.6.6.4 Imaging

Radiographs of the involved area may be warranted to identify arthritis as a possible contributing factor to ganglion cyst development. Ultrasound imaging may be obtained to differentiate between a vascular malformation and ganglion cyst if the clinical exam is not conclusive. Advanced imaging is rarely indicated in the diagnosis of these cysts.

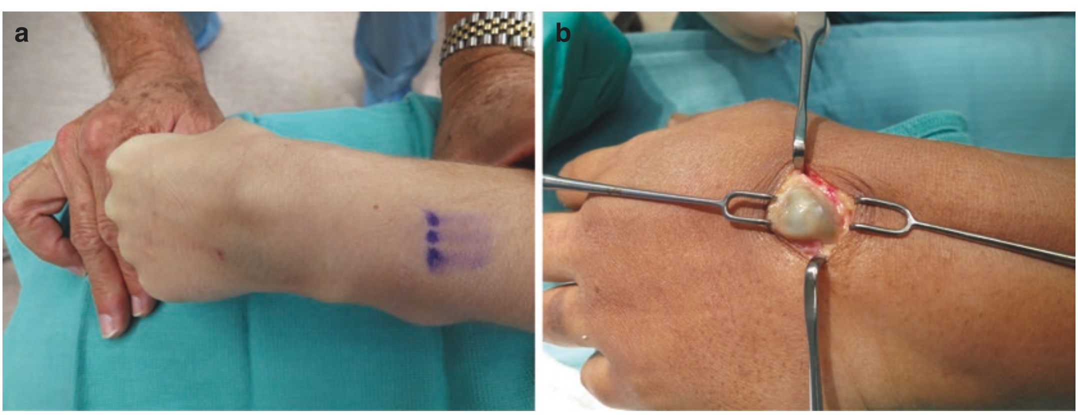

Fig. 27.11 Clinical presentation (**a**) and intra-operative photograph (**b**) of distal wrist ganglion cyst

27.6.6.5 Treatment

These are benign masses and do not inherently require treatment. Common reasons for pursuing treatment are cosmesis and pain that limits activities. Historically, ganglion cysts were treated with closed rupture, either with digital pressure or from the force of a book (hence, the historic name Bible cyst). Unfortunately, this method of treatment was found to have a recurrence rate of approximately 64%. The current mainstay of nonsurgical treatment is aspiration, though this too is associated with a high recurrence rate. Recurrence rates of 50–100% have been found for wrist ganglion cysts, with lower recurrence rates of 30–40% found with aspiration of volar retinacular ganglion cysts. The gold standard for treatment of ganglion cysts is surgical excision. The surgical technique includes excision of the cyst, pedicle, and a cuff of the adjacent joint capsule. With this technique there is a reported recurrence rate of less than 10% [68–70].

27.6.6.6 Complications

The main complication in ganglion cysts is recurrence. As previously discussed recurrence rate can be quite high, so a lengthy discussion with the patient regarding their goals of treatment should be had prior to offering any sort of intervention.

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Common Clinical Conditions of the Hip

28

Joseph Stone

Contents

Goals and Objectives
- *Goal*: To introduce the principles of diagnosis and treatment of structural hip pathology.
- *Objectives*: On completion of this unit, the learner should be able to describe or discuss briefly the following:
  1. Differential of structural hip pathology by age
  2. Key physical exam elements
  3. Diagnostic imaging
  4. Nonoperative management principles
  5. Operative procedures with indications

28.1 Diagnosis of Hip Pain

The diagnosis of "hip pain" can be a clinical challenge as patients may often times be referring to symptoms that are referred from *outside* of the hip (femoroacetabular or ball and socket joint) including the lumbar spine, pelvis (i.e., sacroiliac joints, pubic symphysis), extra-articular soft tissues, or abdomen making an attentive history, focused physical exam, and careful radiographic ordering/interpretation imperative to timely and accurate diagnosis. The scope of this discussion will not include trau-

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matic onset hip pain thereby excluding stress fractures/femoral neck/apophyseal avulsion fractures but should nonetheless be considered in any hip pain differential.

Common Differential Diagnoses (Age-based)
Pediatric

1. Infectious
   (i) Septic Arthritis
   (ii) Osteomyelitis/Periarticular Abscess
2. Inflammatory
   (i) Transient Synovitis
   (ii) Juvenile Idiopathic Arthritis (JIA)
   (iii) Nonbacterial Osteitis (NBO)
3. Structural
   (i) Legg-Calve-Perthes (LCP)
   (ii) Slipped Capital Femoral Epiphysis (SCFE)
   (iii) Dysplasia
   (iv) Femoroacetabular Impingement (FAI)
4. Neoplastic

Adult (>20 years old)

1. Osteoarthritis (OA)
2. Osteonecrosis or Avascular Necrosis (AVN)
3. Inflammatory/Rheumatoid Conditions
4. Lateral Hip Pain
   (i) Greater Trochanteric Bursitis
   (ii) Gluteus Medius Tendinopathy
   (iii) Abductor Insufficiency (Seen in Hip Dysplasia)

28.2 History

Age at presentation is fundamental to working through differential that can broadly be defined as prearthritic vs. arthritic. With an engaged history, it is important to elicit the location of pain, typically having patient point with one finger to the area of maximal perceived discomfort. Inciting event/mechanism, duration, exacerbating and alleviating factors, and pain descriptor (i.e., dull, achy, stabbing, shooting, etc.) are also important to know. Finally, what factor(s) brought the patient to eventually seek care with you as presentation is often NOT acute or timely with patients often seeing multiple providers prior to correct diagnosis.

28.3 Physical Examination

Patients presenting with pain from the abdomen, low back, hip, thigh, or knee should undergo a basic hip examination. The exam is divided into ambulatory, seated, standing, supine, lateral, and prone [1]. This begins with evaluation of the patients' walking/gait with care made to critically assess pelvic position through the gait cycle including a diminished stance phase of gait or limp and foot progression angle [2]. Trendelenburg testing is performed to evaluate abductor insufficiency.

Seated evaluation can allow for evaluation of neurocirculatory conditions and sensitive to FAI. Evaluation of soft tissue elasticity via Beighton score can be helpful to eliminate hypermobility as a potential cause of hip instability [3]. Supine positioning is useful to document hip flexor/abductor strength and subjective irritation from resisted straight leg raise and logroll. The examiner should also use this position to document range of motion both actively and passively with hip flexion/extension and internal/external rotation of the thigh/limb segment.

Palpation of point of maximal tenderness is important especially in laterally based pain as pertrochanteric musculature tenderness is sensitive to abductor fatigue often associated with instability/dysplasia. Tenderness to lateral most aspect of greater trochanter is consistent with greater trochanteric bursitis while pain at the proximal tip of the great trochanter is sensitive to gluteus medius tendinopathy.

28.4 Select Special Tests

Supine

1. *Logroll* – pain with passive internal/external rotation of the hip in extended position (nonspecific).

2. *FABER/Patrick* – pain with passive flexion/abduction, external rotation of the hip positive for sacroiliac, vs. posterior hip pain depending on location.
3. *Anterior apprehension* – positive for anterior hip instability if apprehensive with extension/external rotation of the hip with hemipelvis at table's edge.
4. *Circumduction* – positive for pathologic psoas tendon with painful snapping (internal snapping hip) from flexed/abducted position to extended/adducted position.
5. *FADIR* (flexion, adduction, internal rotation) – sensitive for impingement if painful, typically saved for later in the supine examination given its ability to irritate the hip for subsequent examination.

Lateral position (affected side up)

6. *Bicycle test* – simulated bicycle riding motion with lateral discomfort positive for abductor fatigue often associated with hip instability.
7. *Ober test* – passive extension of affected hip. Failure of patients' limb to cross midline is indicative of tensor fascia lata contracture.

28.5 Diagnostic Techniques

Special diagnostic techniques that may aid in the evaluation of hip pathology are radiography, ultrasonography, advanced imaging (CT and MRI (+/− arthrography), diagnostic/therapeutic injections, and laboratory evaluation.

Structural abnormalities of the hip are uniquely suited to *radiographic examination*. Recognition of normal edge anatomy is essential as inability to do so may lead to diagnostic error. For an adequate study, radiographs should be taken in at least two projections, usually anteroposterior (AP) and lateral.

Routine radiographic examination of the painful hip/limp in a pediatric patient consists of an AP pelvis (standing, if possible) and frog pelvis images [4]. These evaluations have poor sensitivity for transient synovitis, JIA, septic arthritis, or osteomyelitis except for subtle joint space widening in the absence of advanced disease. LCP or Perthes radiographically begins with subtle joint space widening followed by increasing sclerosis of the epiphysis followed by fragmentation and loss of epiphyseal height progressing to new bone formation (reossification) and finally healed femoral head (Figs. 28.1 and 28.2).

The frog lateral radiograph is most sensitive for evaluation of SCFE with disruption of Klein's line typically indicating anterior displacement of femoral neck (metaphysis) in relation to femoral head (epiphysis) (Fig. 28.3).

Initial radiographic evaluation of the painful hip (>12 y/o) consists of standing AP pelvis, false profile, and Dunn 45° radiograph. The AP pelvis and false profile, in general, allow for evaluation

Fig. 28.1 Standing AP pelvis revealing bilateral femoral head increased sclerosis concerning for LCP or Perthes

Fig. 28.2 Standing AP pelvis 7 months lateral revealing advancing femoral head fragmentation with subluxation

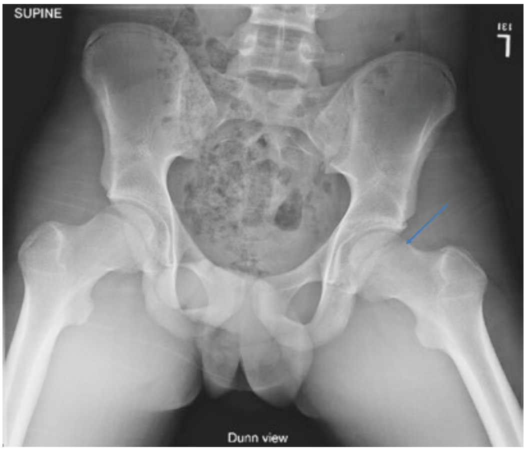

Fig. 28.3 Dunn 45° view used to evaluate femoral-sided FAI (offset disease) (see blue arrow)

Fig. 28.4 Following subcapital realignment

of acetabular morphology [4]. The AP pelvis is used to visualize joint space, relative acetabular coverage, acetabular version or rotation, and femoral head subluxation. The false profile of Lequesne [5] provides an orthogonal view of the acetabulum allowing for anterior acetabular coverage and description of the morphology of the anterior inferior iliac spine [6] which can be a source of extra-articular impingement (Fig. 28.4). The Dunn 45° is used to assess proximal femoral morphology and is considered the most sensitive plain film to assess cam-type FAI [7] (Fig. 28.5).

Magnetic resonance imaging (MRI) allows for multiplanar anatomic evaluation without radiation broadly looking at potential soft tissue inju-

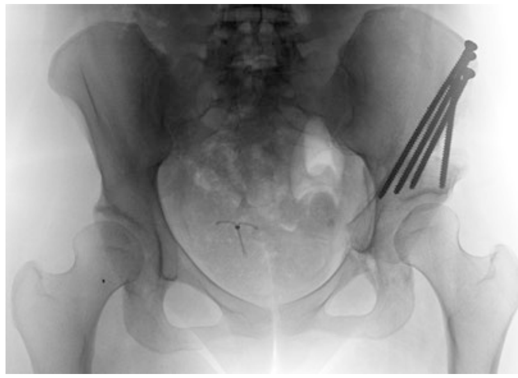

Fig. 28.5 Standing AP pelvis following left Bernese periacetabular osteotomy (PAO)

ries. Conventional MRI is valuable for visualizing femoral head shape, articular cartilage, metaphyseal and epiphyseal changes, and synovitis. It is also considered more sensitive than bone scintigraphy at demonstrating hypovascularity and neovascularization [8]. Contrast-enhanced and diffusion-weighted MRI has been used increasingly in the early detection of LCP and osteonecrosis/AVN allowing for more timely diagnosis with the possibility of improved prognosis and treatment [9, 10].

Ultrasonography is a useful tool for assessing hip joint effusion and/or periarticular fluid collection, and while nonspecific, the absence of joint effusion is helpful at ruling out septic arthritis which is a significantly morbid diagnosis, depending on the virulence of the causative organism. Ultrasound is often helpful in the setting of equivocal physical exam findings. You should consider ordering bilateral hip ultrasound if a negative ultrasound would avoid further imaging and/or aspiration. Ultrasound can be used to guide *arthrocentesis* should removing hip joint fluid be deemed clinically necessary based on clinical picture and laboratory evaluation.

Ultrasound can also be used to guide a*rthrography* which is performed by injecting contrast material into the hip joint. Its greatest value has been in diagnosing labral pathology, and when short- and medium-acting local anesthetics are added to the "cocktail," a *diagnostic/therapeutic injection* can add to the diagnostic capacity of the exam as failure to resolve any of patients' hip

pain would reveal that the source of the hip pain is likely not intra-articular.

Computerized axial tomography (CAT) is a noninvasive radiographic technique that often provides better boney pathologic definition than conventional radiographs specifically in the setting of SCFE and prior operated pelvis. For this reason, they are employed frequently to facilitate the diagnosis and management of select hip injuries.

Arthroscopy is also a valuable diagnostic and therapeutic modality capable of managing a significant amount of intra-articular pathology including SCFE/FAI and its *early* sequelae including chondral and labral injury. The arthroscope, which permits direct visualization of much of the joint, can be very helpful in elucidating intra-articular pathology.

Laboratory evaluation may be useful in delineating infections from inflammatory pathology so, in the presence of atraumatic hip pain with associated fever and limp, it's advisable to begin with a complete blood count (CBC) with differential, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). If infection is suspected, arthrocentesis fluid should be sent for cell count and gram stain. If infection and structural abnormalities have been ruled out, basic inflammatory markers including rheumatoid factor and human leukocyte antigen B27 can be ordered with consideration of rheumatology referral.

28.6 Treatment

Treatment of septic arthritis and periarticular abscesses is focused on timely decompression followed by targeted antibiotic management with consideration of involvement with infectious disease providers. Osteomyelitis can often be managed exclusively with antibiotics assuming focal subperiosteal/intraosseous abscess do not exist.

Treatment of inflammatory conditions like transient synovitis begins with nonsteroidal anti-inflammatory drugs and careful observation/close monitoring to ensure appropriate clinical response with typical course being progressive resolution in hours to days. With conditions such as JIA and NBO, once diagnoses have been made, long-term care is typically handled by rheumatology with titration of glucocorticoids, disease-modifying antirheumatic drugs, bisphosphonates, and tumor necrosis factor alpha antagonists used to a desired clinical effect.

Multiple interventions exist for the management of LCP depending on patients' age at onset of disease, hip motion, phase of disease (pre- or post-collapse) (Figs. 28.1 and 28.2), and patient/surgeon preference. The menu consists of activity modification, stretching, physiotherapy, limited weight-bearing, Petrie casting, +/− adductor tenotomy, varus proximal femoral osteotomy, arthrodiastasis, and triple innominate osteotomy with the goal of *containing* the femoral head at risk for deformation. This deformation often leads to FAI plus possible instability in the healed stage leading to early OA. In the setting of healed Perthes-like disorders, treatment options include shelf osteotomies, valgus extension proximal femoral osteotomy, and relative neck lengthening through a surgical dislocation approach (Figs. 28.6 and 28.7).

SCFE management depends on a number of factors including acuity of pain (> or <3 weeks), stability (can a patient walk or not), and what is the degree of the slip deformity. While current "gold standard" is in situ screw fixation, dual-screw fixation is recommended in the setting of physeal instability. Other options include in situ screw fixation with open vs. arthroscopic osteo-

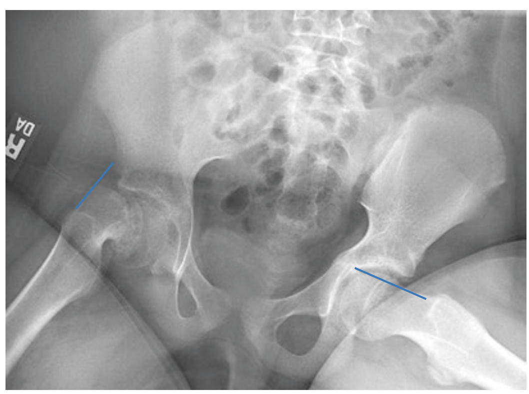

Fig. 28.6 Supine AP pelvis revealing right severe slipped capital femoral epiphysis (SCFE). Klein's line (in blue): not touching the femoral head consistent with SCFE

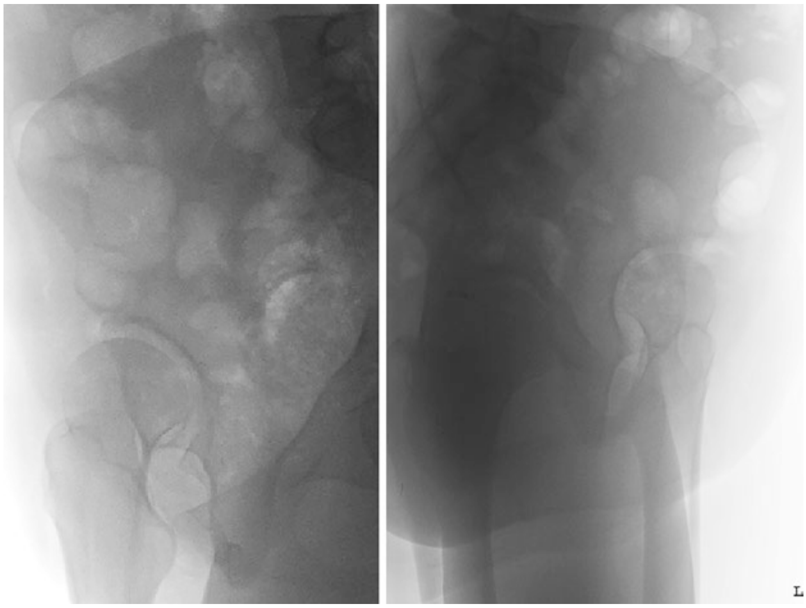

Fig. 28.7 Bilateral false profile imaging revealing anterior undercoverage bilaterally seen in dysplasia

Fig. 28.8 Standing AP pelvis revealing “healed” Perthes-like deformity of the right femoral head

Fig. 28.9 Standing AP pelvis revealing healed Perthes-like deformity of the right femoral head. Following surgical hip dislocation with relative neck lengthening

plasty to remove the impinging metaphysis. Osteotomy options from the intertrochanteric region to the subcapital region including modified Dunn subcapital realignment have been described with varying degrees of survival and AVN risk (Figs. 28.3, 28.8, and 28.9).

Hip dysplasia management is primarily driven by age at diagnosis as untreated; it is the cause of 67% female OA previously thought to be idiopathic [11]. Early intervention consists of harnesses and braces progressing to closed repositioning and open reduction +/− femoral shortening and pelvic osteotomies with casting. In the adolescent and prearthritic adult population, the Bernese periacetabular osteotomy is an increasingly utilized intervention with 76% survival (no conversion to total hip arthroplasty and “low” pain scores in most recent medium-term follow-up) [12] (Figs. 28.10 and 28.11).

Management of FAI depends on the cause of the impingement being the femoral head/neck junction (cam impingement), the acetabulum (pincer impingement), or most commonly a com-

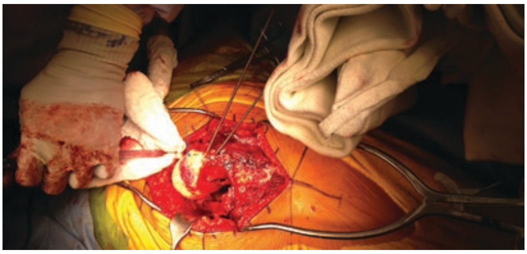

Fig. 28.10 Intraoperative SCFE imaging revealing temporary stabilization of the femoral head prior to reorientation. Blue arrow: avulsed periosteum

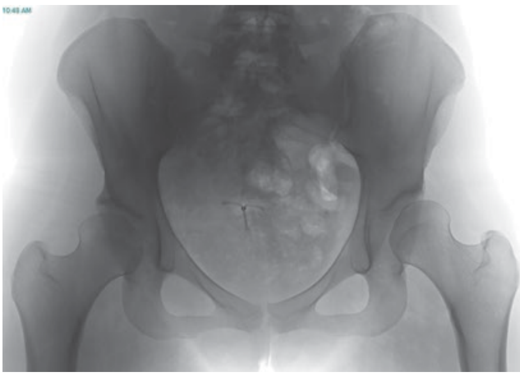

Fig. 28.11 Standing AP pelvis revealing bilateral hip dysplasia in skeletally mature female

bination of the two [13]. Management options include arthroscopic vs. open osteoplasty of the dynamically impinging structure or osteotomy/derotation of either the acetabulum or the femur with subsequent dynamic assessment to ensure no intra- or extra-articular impingement lesions exist.

Symptomatic hip osteoarthritis recalcitrant to diet, exercise, activity modification, possible corticosteroid injections (CSI), and over-the-counter medications with controlled medical comorbidities remains a good candidate for a total hip arthroplasty. This is the preferred treatment for older symptomatic patients with advancing arthritic changes. Other options include femoral and acetabular osteotomies depending on location and severity of the OA, femoral head resurfacing, hip fusion, and femoral head resection.

Osteonecrosis or avascular necrosis (AVN) is an especially challenging diagnosis with multiple direct and indirect causes. Nonoperative treatment options include bisphosphonate medications for pre-collapse AVN [14]. Operative treatment includes core decompression vs. multiple epiphyseal drilling with or without bone grafting. Rotational osteotomies and curettage and bone grafting techniques have been described for smaller lesions. Vascularized free-fibula transfers have been described to support subchondral bone to mitigate/prevent collapse. As in other advanced degenerative hip conditions, hip resurfacing, total hip arthroplasty, and hip fusion are options based on age, severity, and patient/surgeon preference.

Lateral hip pain differential continues to grow with a better understanding of anatomy, and nonsurgical methods are the mainstay of treatment. While CSI continue to be helpful for true greater trochanteric bursitis, refractory cases may be candidates for open bursectomy. External snapping hip from thickened iliotibial band dynamically passing over the lateral most aspect of the greater trochanter recalcitrant to rest, and physical therapy may consider Z-plasty or release. Hip abductor tears that fail to respond to NSAIDs, PT, and CSI may consider open vs. "arthroscopic" repair of partial- and full-thickness tears. Lateral hip pain with vague abductor fatigue warrants critical evaluation of radiographs to rule out acetabular dysplasia as cause of abductor fatigue leading to possible need for Bernese periacetabular osteotomy.

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Common Clinical Conditions of the Knee

29

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Contents

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Goals and Objectives

- *Goals*: To familiarize readers with basic anatomy and biomechanics of the knee and associated injuries and to provide basic diagnostic and treatment options.
- *Objectives*: On completion of this unit, and using this syllabus as a standard reference, the learner should be able to evaluate, describe, or identify the following:
  1. General anatomic structure and biomechanics of the knee
  2. Understand the composition and role of each of the following:
     A. Articular cartilage
     B. Meniscus
     C. Anterior cruciate ligament
     D. Posterior cruciate ligament
     E. Medial collateral ligament
     F. Lateral collateral ligament
  3. Understand diagnosis and treatment of osteoarthritis
  4. Understand diagnosis and treatment of conditions affecting the following:
     A. Patella
     B. Meniscus
     C. Cruciate ligaments
     D. Collateral ligaments

29.1 Basic Knowledge of the Knee

29.1.1 Anatomy

The knee is a hinged joint, which also allows for some translational and rotational movement. The femoral condyles articulate with the tibial plateau to form the basic structure. Additionally, the proximal fibula forms a joint and serves as an origin or insertion site for lateral knee joint stabilizers. The articulating surface of the distal femur and the proximal tibia are covered with articular cartilage, which functions to protect and lubricate the joint. Attached to the tibial plateau, the medial and lateral menisci provide stability and protection in the form of shock absorbers and joint nutrition [1]. The patella rests anteriorly and is the largest sesamoid bone in the body [2]. It serves as an anchor point for the quadriceps and patellar tendons and facilitates the action of the extensor mechanism. A number of ligamentous attachments further stabilize the knee. Found within the joint, specifically in the intercondylar notch of the femur, is the anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL). The medial collateral ligament (MCL) is the primary stabilizer medially, while the lateral collateral ligament (LCL) is lateral. While MRI is often needed to evaluate injuries around the knee, the imaging evaluation of most patients will begin with plain radiographs (Figs. 29.1 and 29.2).

Fig. 29.1 Normal anteroposterior (AP) and lateral radiographs of the knee. Plain radiography is the modality of choice for the initial imaging evaluation of most patients with knee injuries

Fig. 29.2 Normal anteroposterior (AP) and lateral radiographs of the knee. Plain radiography is the modality of choice for the initial imaging evaluation of most patients with knee injuries

29.1.2 Biomechanics of the Knee

Normal range of motion of the knee is from a few degrees of hyperextension to 130° of flexion. In full extension, there is essentially no rotation or translational motion. However, when the knee is flexed to 90°, give within the ligaments allows internal rotation of 35° and external rotation of 45°. Similarly, at 30° of flexion, a few degrees of motion is normal with varus and valgus stress. When in extension, the anterior femoral condyle is in contact with the tibial plateau, and as the knee flexes, the contact point shifts posteriorly. In addition, as the knee approaches full extension, the tibia undergoes approximately 10° of external rotation over the final 20° of knee extension. This rotation is a product of the mismatched contour of the femoral condyles and tensions the collateral and cruciate ligaments to limit motion at full extension [2].

29.2 Meniscus

29.2.1 Anatomy and Function

The knee has two menisci – the lateral and medial meniscus – which are crescent-shaped fibrocartilaginous structures with a triangular cross section. The menisci are primarily composed of type I collagen fibers but are up to 75% water in overall composition. In addition, types II, III, V, and VI are also present in smaller quantities. Intimate with the composition of water are proteoglycans, which are considered hydrophobic [3]. Each of the medial and lateral menisci has anterior and posterior root attachments to the tibia [4]. Only a portion of the menisci receive direct blood supply from the geniculate arteries, and this portion changes over time. In adulthood, 25% or less of menisci receives direct blood supply, while the majority is nourished via diffusion. Effectively, each meniscus is divided into regions related to vascularity, with the most peripheral region receiving direct nourishment. Anteriorly, the menisci are attached via the transverse intermeniscal ligament. Meniscofemoral ligaments further stabilize the lateral meniscus posteriorly, emanating from the posterior horn of the meniscus and attaching to the PCL and medial femoral condyle [1]. The lateral meniscus covers greater than 80% of the tibial condyle and is circular and only loosely attached to surrounding soft tissues and knee capsule. In direct contrast, the medial meniscus covers around 60% of the tibial condyle, is more C-shaped, and exhibits less excursion owing to its strong attachments to the medial joint capsule.

The primary function of the meniscus is distribution of the load across the knee joint. In extension, the menisci collectively transmit 50% of forces, while in flexion, they transmit 85% of forces. It serves to increase the contact area between femur and tibia and decreases the

contact between the articular cartilage surfaces. They also play an important role in stability, joint lubrication, and joint congruity and contribute to limits of flexion and extension [4]. As such, the orientation of collagen fibers is best characterized as a network to help fulfill these important roles. Fibers are oriented radially, circumferentially, and longitudinally, to resist forces in all planes. Additionally, strong attachments on the anterior and posterior horns also allow the meniscus to fulfill their functions. Similarly, the loose peripheral attachment of the lateral meniscus allows more excursion. The meniscus serves as a shock absorber by dispersing the axial loads via the circumferential fibers, otherwise understood as "hoop stresses." The compressive forces of the meniscus are made possible via the movement of water in and out of the matrix of the meniscus [1].

Collectively, the menisci account for the femoral rollback as the knee flexes from 0 to 120. In order for the menisci to accommodate this motion, they translate from anterior to posterior. Specifically, the medial meniscus translates 5 mm while the lateral meniscus translates 11 mm.

Fig. 29.3 T2-weighted MRI image of a posterior horn medial meniscus tear

29.2.2 Injury Diagnosis and Treatment

Meniscus injuries are very common and have been reported as 60–70 per 100,000 per year [5]. There is a slight tendency toward males sustaining injuries to the meniscus compared to females, with a peak occurring in the third decade in males and second decade of life in females. Medial meniscus tears occur more commonly, at least in part due to the increased constraint of the meniscus, although lateral tears occur more commonly with ACL injuries [6]. The mechanism for injury is usually a combination of axial loading and rotational forces, which leads to shearing of the meniscus. Acute or traumatic tears occur in younger, more active individuals while a degenerative tear typically results in the setting of cartilage wear. Injuries are typically associated with pain and varying degrees of swelling (Fig. 29.3) [1]. Mechanical symptoms, such as locking, clicking, grinding, or feelings of instability, can often correlate with the size and characteristics of the tear. Specifically, tears are classified as longitudinal (vertical), radial, horizontal (cleavage), flap, bucket handle, and degenerative.

Occasionally, meniscal variants such as a discoid meniscus can contribute to pathology. In these situations, instead of the meniscus being crescent-shaped, it can be more of a half-moon in shape or sometimes an almost complete circle of fibrocartilage. Despite the aberrant development of the meniscus, many patients can remain asymptomatic throughout their life.

Injuries to the meniscus can be suspected through a careful history and physical exam. Discussing the mechanism of the injury can provide considerable information when trying to determine the problem. Radiographs can provide additional information, and the reviewer can infer injury to the meniscus by way of the remaining joint space, presence of osteophytes, loose bodies, and degenerative changes. However, to fully assess the appearance of the meniscus, MRI is the imaging modality of choice [7]. Careful evaluation of this study can provide information regarding the presence and characteristic of pathology

and establish appropriate treatment plans. Surgical treatment is primarily arthroscopic and can include meniscus trimming (meniscectomy), repair, and transplantation.

29.3 Anterior Cruciate Ligament

29.3.1 Anatomy and Function

Found within the intercondylar notch is the anterior cruciate ligament (ACL), which is comprised of two distinct bundles consisting almost entirely of type 1 collagen [8]. The ACL has an anteromedial and posterolateral bundle and attaches to the posteromedial aspect of the lateral femoral condyle within the notch. On the tibia, it attaches to the anterior aspect of the plateau, just anterior and slightly medial to the intercondylar eminence [8].

The primary function of the ACL is to resist anterior translation of the tibia, in relation to the femur. Additionally, it serves as a secondary role resisting internal rotation of the tibia and as a restraint to varus and valgus stress. The anteromedial bundle of the ACL is considered stronger and tightens with the knee in flexion, while in extension, the posterolateral bundle becomes taut.

29.3.2 Injury Diagnosis and Treatment

A careful history from a patient who sustains an injury to the ACL can alert the examiner to the source of the problem. More commonly (~2/3), an injury to the ACL is via a noncontact mechanism including jumping, cutting, or sudden change of direction. The remaining injuries typically result from a direct blow, often causing the knee to hyperextend or create a significant valgus stress. A popping sound is frequently heard or felt by the individual. Substantial swelling of the knee happens almost immediately as a result of the direct blood supply from the middle geniculate artery. Physical exam testing reveals increased anterior translation of the tibia compared to the contralateral knee. The Lachman test has an 85% sensitivity and a 94% specificity in detecting ACL injuries [9]. Radiographs can evaluate for fractures, loose bodies, or other associated injuries. However, an avulsion fracture off the lateral tibial condyle is referred to as a segond fracture and is pathognomonic for an ACL injury. More recent evidence suggests this avulsion may in fact be an avulsion of the anterolateral ligament. If injury to the ACL is suspected, an MRI is obtained, which allows for direct evaluation of both bundles of the ACL, as well as associated injuries. An MRI has a sensitivity or 86–95.9% and specificity of 91–95% although clinical suspicion and exam could be sufficient for diagnostic arthroscopy (Figs. 29.4 and 29.5) [9].

Fig. 29.4 MRI images demonstrating ACL injury. Figure 29.4 is a sagittal MRI image with deficient ACL. Figure 29.5 is a T2-weighted image showing associated knee effusion and bone bruise of the lateral condyle of the femur

29.4 Posterior Cruciate Ligament

29.4.1 Anatomy and Function

Also found within the intercondylar notch is the posterior cruciate ligament (PCL). Two bundles form the PCL including an anterolateral and pos-

Fig. 29.5 MRI images demonstrating ACL injury. Figure 29.4 is a sagittal MRI image with deficient ACL. Figure 29.5 is a T2-weighted image showing associated knee effusion and bone bruise of the lateral condyle of the femur

teromedial bundle. These bundles are also made almost entirely of type 1 collagen. It attaches to the anterolateral aspect of the medial femoral condyle, and to the posterior aspect of the tibia, 10–15 mm below the posterior articular surface.

The PCL primarily resists posterior translation of the tibia in relation to the femur and also serves to resist external rotation of the tibia as well as varus angulation of the tibia. The anterolateral bundle is twice the size of the posteromedial bundle, with greater stiffness and strength. This bundle tightens in knee flexion, whereas the posteromedial bundle tightens with extension [10].

29.4.2 Injury Diagnosis and Treatment

Injuries to the PCL can often go undiagnosed, so the precise incidence is not well understood. As such, PCL tears represent less than 5% of reported injuries in college soccer, professional football, and college basketball [11]. Most commonly, injuries to the PCL are caused by posterior-directed forces to the proximal tibia, often during sports or a motor vehicle collision. Similarly, hyperflexion or hyperextension of the knee can lead to PCL damage. The former mechanism is most likely to result in an isolated PCL injury, which is rare considering that 90% of traumatic injuries to the PCL are in the setting of concomitant injuries. It is estimated that 60% of the concomitant injuries include damage to the posterolateral corner (PLC) of the knee [12]. Unlike an ACL tear, there is typically not a "pop" associated with a PCL tear. More frequently, patients complain of posterior knee pain, pain with kneeling, or general stiffness related to swelling. Patients may also complain of instability, or a general sense that something is wrong with the knee. Physical exam alone is 96% accurate with posterior drawer testing being the most effective, having a sensitivity of 90% and a specificity of 96%. If concerned about a combination of PCL and PLC injury, the dial test can be used to help distinguish which structures may be affected. MRI is used to evaluate the PCL and any additional injuries and has a sensitivity of 96%, with a specificity of 100% [10]. Surgical treatment of PCL injuries remains controversial and often follows a period of nonoperative treatment. PCL tears in conjunction with ACL or PLC injuries are often treated with surgery, while isolated injuries depend largely on activity levels of the patient and severity of the injury.

29.5 Posterolateral Corner

29.5.1 Anatomy and Function

Collectively, the arcuate ligament, lateral collateral ligament (LCL), popliteus tendon, popliteofibular ligament, lateral gastrocnemius tendon, and the posterolateral knee capsule comprise the PLC complex. These structures serve as a restraint to varus stress, external tibial rotation, and posterior translation of the tibia [10]. The LCL is the primary restraint to varus stresses while the entire complex is

responsible for resistance to external tibial rotations and posterior tibial translation. In isolation, injuries to the PLC are rare but have been reported in greater than 60% of injuries to the PCL, 87% of multiple ligamentous injured knees, and 68% of tibial plateau fractures [13–16]. As such, a high index of suspicion is necessary in order to accurately diagnose injuries to the PLC. In fact, 72% of injuries to the PLC were initially missed, with an average delay to diagnosis of 30 days [17].

In cases where damage to the PLC goes undiagnosed, knees are at an increased risk of early-onset osteoarthritis. Similarly, in knees requiring ACL or PCL reconstruction, failure to diagnose injury to the PLC is associated with graft failure, if damage to the PLC is not addressed.

29.5.2 Injury Diagnosis and Treatment

As previously mentioned, injuries to PLC are frequently missed, so a focused physical exam is crucial for diagnosis. At the same time, a thorough understanding of the mechanism can alert the clinician as to the possibility of associated injuries to the PLC. The dial test compares the rotational profile about the knee, and careful utilization can distinguish between an isolated PLC injury and a combined PLC/PCL injury. Varus stressing of the knee can also provide evidence of an LCL injury.

Radiographs can be helpful in identifying potential injury to the PLC complex. Lateral joint line widening is indicative of increased varus laxity, especially with stress views. Additionally, fibular head/tip avulsion fractures, Gerdy's tubercle fractures in iliotibial band injuries, tibial plateau fractures, or segond fractures can all indicate a potential injury to the PLC.

As is the case with other ligamentous injuries to the knee, MRI can be a valuable diagnostic tool. However, in comparison, MRI is not as sensitive in identifying injuries to the PLC in some cases. For example, MRI carries a sensitivity of 93% if used within 12 weeks of the injury, but this decreases to 26% if imaging is delayed greater than 12 weeks.

29.6 Medial Collateral Ligament

29.6.1 Anatomy and Function

Found on the medial aspect of the knee, spanning from the distal femur to the proximal tibia, the medial collateral ligament (MCL) consists of superficial and deep attachments. In addition, the posterior oblique ligament extends from the distal semimembranosus tendon and provides additional stability to the medial knee. The superficial MCL has a single proximal attachment to the distal femur and two attachments distally on the proximal tibia. Attaching approximately 12 mm from the tibial joint line, the most proximal tibia attachment is to the anterior aspect of the semimembranosus tendon, while the distal tibial attachment extends an average of 61 mm distal to the joint line, attaching just anterior to the posteromedial tibial crest. The deep MCL is a medial knee capsular thickening and consists of meniscofemoral and meniscotibial ligaments. The meniscofemoral ligament is longer, while the meniscotibial ligament is shorter and thicker [18].

The MCL is the primary restraint to valgus forces and secondarily resists external and internal tibial rotation, as well as posterior tibial translation. The greatest resistive force to valgus stress is provided by the superficial MCL. Beyond 30 degrees of flexion, the superficial MCL also provides the most resistance to rotational forces, as the posteromedial knee capsule becomes slack. In contrast, with the knee in extension, the posteromedial capsule is taught and provides additional resistance to valgus and rotational stress. The deep MCL provides no additional stability to the medial knee, provided the superficial MCL remains intact, as determined by cadaver studies [19].

29.6.2 Injury Diagnosis and Treatment

As is the case for other ligamentous knee injuries, a careful history can provide information for diagnosis of a medial knee injury. Any valgus-directed blow or force on the knee can result in an MCL injury. On physical exam, malalignment of the knee, swelling, and gait abnormalities can be observed. Additionally, tenderness over the medial knee, at the site of proximal and distal MCL attachments, is often indicative of an injury. Tenderness along the medial joint line could indicate an associated meniscus injury. Valgus stress of the knee should be tested at 0 and 30 degrees of knee flexion in order to assess the contribution of the posteromedial capsule. Radiographs can be used to evaluate malalignment, especially on weight bearing x-rays. MRI can be used to evaluate for additional soft tissue injuries, as well as to determine the severity of injury to the MCL.

Oftentimes, MCL injuries can be treated nonoperatively with protected weight-bearing and gradual return of range of motion. Numerous factors including overall alignment, associated injuries, chronicity of the injury, and instability are considered. Treatment options depend on the whole clinical picture and can range from repair to medial soft tissue tensioning to reconstruction with and without augmentation.

29.7 Osteoarthritis

29.7.1 Articular Cartilage

Articular or hyaline cartilage is found at the articular surfaces of the distal femur and proximal tibia. It functions to distribute loads across the joint and decreases friction [20]. Cartilage is composed of extracellular matrix and cells. The majority of the extracellular matrix is composed of water (up to 80%) which provides the bulk of the mass. An additional 10–20% of the dry weight is composed of type II collagen (90–95%) with some contribution from other collagen types and provides the framework for cartilage and tensile strength [21]. Proteoglycans, primarily chondroitin sulfate and keratin sulfate, are the final component of the ECM. These molecules function to increase the compressive strength of cartilage and attract water. Chondrocytes represent the cellular component of cartilage. These are derived from chondroblasts that are trapped within lacunae and become chondrocytes. They serve a number of functions including collagen and proteoglycan production, as well as enzymes necessary for regular metabolism [5, 22].

29.7.2 Progression of Osteoarthritis

Osteoarthritis is defined as a degenerative disease of synovial joints that results in progressive damage and subsequent loss of articular cartilage. Annually, 240 per 100,000 individuals are diagnosed with symptomatic knee arthritis [23]. Wear and tear arthritis or osteoarthritis is by far the most common form of arthritis and can be affected by a number of modifiable and non-modifiable risk factors. In particular, a history of trauma to the knee, obesity, repetitive knee bending (occupational), and metabolic syndrome are all modifiable and can lead to an increased risk of arthritis. Similarly, females tend to be affected more than males, as do older patients. Genetics and race can also influence the development and progression of arthritis. In early stages of arthritis, an insult to cartilage leads to damage and results in increased water content and composition of proteoglycans. Collectively, these changes affect the properties of the cartilage and disrupt the organization and orientation of the collagen fibers. As the disease process progresses, the synovium undergoes changes starting with mild inflammatory changes and leading to increased vascularity and thickening of the synovium. In response, the subchondral bone attempts to remodel, leading to sclerotic bone formation and bone spurs on radiographs (Fig. 29.6). In addition, excess synovial fluid is produced in an attempt to lubricate the joint, leading to an effusion. Patients with osteoarthritis can exhibit a wide variety of symptoms including debilitating

Fig. 29.6 Standing radiograph of a patient with bilateral knee osteoarthritis. Note the overall alignment (varus or "bow-legged") and loss of normal articular space

knee pain, worsening pain at night or rest, swelling associated with level of activity, knee stiffness, and feelings of instability related to mechanical catching and locking. As symptoms worsen, the overall alignment of the leg can be affected, resulting in varus or valgus deformities about the knees.

29.7.3 Diagnosis and Treatment

Careful history and physical information can help to establish a diagnosis, without the need for radiographs. However, to accurately assess the severity of osteoarthritis, radiographs provided invaluable information. Typically, weight-bearing XR are preferred and knees affected with osteoarthritis can demonstrate medial, lateral, and patellofemoral joint involvement. Commonly, joint space narrowing, osteophytes, sclerosis, bone loss, and overall joint malalignment can be indicative of osteoarthritis.

Treatment options are largely dependent on the severity of presenting symptoms. Initial treatments are utilized for symptomatic control and include NSAIDs, steroid injections, bracing, and weight loss. Should symptoms persist, leading to

Fig. 29.7 Anteroposterior (AP) radiograph of a patient after a total knee arthroplasty (knee replacement)

a progression of symptoms and worsening appearance on radiographs, consideration for surgery is warranted. In the event of malalignment, specialized surgeries involving osteotomies can realign the healthy joint surfaces, effectively offloading the affected portion of the hip joint. If other treatment options fail to provide sustained relief, a total or partial knee replacement can be used to improve alignment and overall function (Fig. 29.7).

29.8 Knee Extensor Mechanism

Collectively, the quadriceps tendon, patellofemoral joint, patellar tendon, and tibial tubercle make up the knee extensor mechanism (Fig. 29.8) [24]. Complete injury to any of these structures can have significant functional consequences resulting from the inability to extend the knee and to stabilize the extremity during stance phase of normal gait.

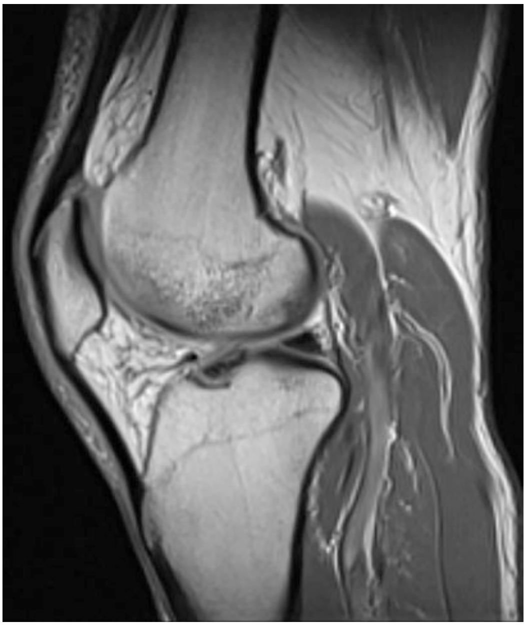

Fig. 29.8 Normal sagittal MRI image showing intact knee extensor mechanism including normal quadriceps tendon, patella, and patellar tendon

Fig. 29.9 Sagittal MRI image of a patient with a quadriceps tendon rupture

29.8.1 Quadriceps Tendon Rupture

The most proximal portion of the knee extensor mechanism is the quadriceps tendon, which is the confluence of tendons from the rectus femoris and the three vastus muscles. Ruptures of the quadriceps tendon are relatively rare, occurring in 1.37/100,000 patients per year, and they tend to affect middle-aged males predominantly [25]. Typically, ruptures occur following direct or indirect trauma, usually following a sudden forceful eccentric contraction of the quadriceps tendon. Occasionally, spontaneous ruptures occur, but these are usually in patients with comorbidities including chronic renal failure, rheumatoid arthritis, diabetes, gout, and abuse of steroids and can even lead to bilateral injuries [26]. There are case reports of spontaneous bilateral ruptures in healthy, active individuals, but these types of bilateral injuries are exceedingly rare [27]. Commonly, patients will complain of severe pain experienced after trying to maintain balance while attempting to avoid a fall. Clinically, patients will complain of acute onset pain, a palpable defect proximal to the patella, and inability to actively extend the knee or maintain a straight leg raise. Imaging, including ultrasound and MRI (Fig. 29.9), can be used to confirm a diagnosis, but ruptures of the quadriceps tendon are often diagnosed based on history and clinical exam. Early operative repair is imperative to restore the function and range of motion. Numerous repair techniques have been reported, and all have been determined to be successful; however no method has been determined to be superior to date [28, 29].

29.8.2 Patellar Tendon Rupture

The patellar tendon extends from the inferior pole of the patella to the tibial tubercle. It is the most distal aspect of the knee extensor mechanism. Ruptures represent the most common acute injury but remain relatively uncommon, occurring in 0.68/100000 [25]. Injuries affect males more than females and is more commonly seen in patients younger than 40. Three standard patterns of disruption include avulsion from the inferior pole of the patella, midsubstance of the tendon, or distally from the tibial tubercle. Ruptures occur as an avulsion with or without bone from the inferior patella or tibial tubercle. Traumatic ruptures typically result from a strong eccentric contraction of

Fig. 29.10 T1- and T2-weighted sagittal MRI images of a patient with a patellar tendon rupture. Note the significant edema around the tendon on the T2 image

Fig. 29.11 T1- and T2-weighted sagittal MRI images of a patient with a patellar tendon rupture. Note the significant edema around the tendon on the T2 image

the quadriceps and can affect the patellar tendon in younger patients, as it is an extension of the quadriceps. However, rupture requires a high amount of force, estimated to be 17.5 times the body weight [30]. In contrast, ascending stairs generates forces equivalent to 3.2 times the body weight [31]. As such, preexisting conditions that are known weaken collagen, such as systemic lupus erythematosus, rheumatoid arthritis, and chronic renal failure, and diabetes can weaken tendons, leading to atraumatic ruptures [32]. Similarly, primarily related to forces required to cause rupture, previous studies have demonstrated preexisting pathology prior to an acute event [33]. Patients will present complaining of pain in the anterior knee, unable to extend the knee. On exam, a palpable defect will be present distal to the knee. Radiographs can provide additional support in the way of a high riding patella, or patella alta. Ultrasound and MRI (Figs. 29.10 and 29.11) can also be used to support a diagnosis, although, much like quadriceps tendon ruptures, patellar tendon ruptures tend to be a clinical diagnosis. In an attempt to regain full function, early surgery is recommended. Direct repair in the acute period has good results, with primary repair the most common approach. Once again, multiple methods exist, but heavy suture and direct repair of the injured tendon are the goal. Delayed repair or chronic ruptures requiring reconstruction have worse results, although function still remains good [32].

29.8.3 Patellar Fracture

The patella is the largest sesamoid bone in the body, lying within the sling created by the quadriceps and patellar tendon. As such, the "kneecap" increases the mechanical advantage of the quadriceps, contributing to the muscles' capacity to generate forces five times greater than the body weight [34]. Complete fracture of the patella can therefore disrupt the knee extensor mechanism (Figs. 29.12 and 29.13). Fractures involving the patella can be classified according to the morphology, amount of displacement, location, and number of fractures, i.e., comminuted. When the knee flexes, the posterior surface of the patella engages the anterior tibia within the trochlea. On the posterior patella, the articular cartilage is the thickest in the body, up to 1 cm thick [35]. Fractures to the patella can occur via direct contact such as a blow to the knee or indirectly via contraction of the strong quadriceps

Fig. 29.12 AP and lateral radiographs of a patient with a patellar fracture

Fig. 29.13 AP and lateral radiographs of a patient with a patellar fracture

muscle. The fracture can extend medially and laterally through the retinaculum, leading to displacement [35]. Evaluation of a patient with a suspected patella fracture demonstrates tenderness and bruising. Thorough examination of the extensor mechanism is important as this can influence the decision to treat with surgery. Repair of patella fractures can improve function but can also lead to stiffness and residual pain and arthritis. Various methods can be used to repair the fracture, depending on the characteristics of the fracture.

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Common Clinical Conditions of the Foot and Ankle

30

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Goals and Objectives

- *Goal*:
  - Familiarize the reader with relevant orthopedic clinical anatomy of the foot and ankle
  - Provide a framework for understanding common ailments of the foot and ankle
  - Introduce the reader to the basic physical examination of the foot and ankle
- *Objectives*:

  On completion of this unit, the learner should be able to:
  1. Perform a physical exam of the foot and ankle in the ambulatory setting
  2. Understand and order appropriate imaging in the workup of foot and ankle pathology
  3. Be familiar with common nonsurgical modalities for common ailments
  4. Understand and describe common degenerative, neuropathic, and soft tissue problems in the foot and ankle

30.1 Physical Examination of the Foot and Ankle

30.1.1 Overview

Learning the physical exam of the foot and ankle requires consistency and practice. The foot and ankle play critical roles in locomotion; assessment of gait and standing alignment is paramount. Inspection can also reveal systemic pathologies. This section will discuss physical examination based on anatomic regions of the foot and ankle.

30.1.2 Inspection

As a general rule, the patient does not need to change into a gown or shorts unless the proximal lower extremity alignment is of particular concern. While the patient stands in front of the examiner, the alignment of the foot and ankle can be assessed from both anteriorly and posteriorly.

30.1.3 Standing Examination

In stance, the clinician can appreciate alignment and symmetry. Overall leg alignment should be examined by estimating pelvic tilt with fingers placed on the anterior superior iliac spine, as well as assessing varus or valgus alignment at the ankle, hindfoot, and the knee. Varus and valgus alignment of the heel can be appreciated from posteriorly, as well as a “too many toes sign” in planovalgus alignment, when the lesser toes are visible lateral to the heel from posteriorly [1] (Fig. 30.1). The rotational axis of the ankle may be estimated by placing fingers on either malleolus and exam-

Fig. 30.1 Posterior view of both ankles showing bilateral planovalgus alignment. This finding demonstrates visibility of most of the lesser toes—this finding is referred to as the “too many toes” sign

ining in relation to the tibial tubercle. Asking the patient to rise up on to the toes can help assess the strength of the posterior tibialis (PT, the heel should normally invert into varus as the patient plantar flexes). This ability is also dependent on normal function of the subtalar joint.

Viewed from laterally, the longitudinal foot arch may be examined relative to the contralateral side. Calcaneal position may be neutral, valgus, or varus aligned relative to the tibia (e.g., in heel varus, the medial border of the calcaneus will be visible from the front). In disorders of the longitudinal arch, it is important to note how the foot "tripod," demarcated by the 1st metatarsophalangeal (MTP) joint, the 5th MTP joint, and the plantar posterior heel, is affected by the combination of forefoot adduction and abduction and heel alignment.

The Coleman block test is an in-office examination method for testing the cause of cavovarus foot alignment. As described, it is performed by placing a 1-inch block under the heel and lateral border of the foot and then increasing or decreasing the height of the block in increments until the medial foot rests on the floor [2]. A flexible hindfoot will correct with this method; a rigid hindfoot will not.

30.1.4 Gait Examination

Gait should be examined through many strides with the arms swinging freely. The examiner should look at the whole body, noting that the shoulders should rotate 180° out of phase with the pelvis in the absence of pelvic, spinal, or shoulder pathology. Each phase of gait, stance and swing, should be examined. For the foot and ankle, note the degree of in-toeing, pronosupination, and heel inversion. In normal swing phase, the foot internally rotates roughly 15° and achieves external rotation by the time of toe-off. The foot typically pronates with weight bearing during the first half of stance phase and remains pronated as the heel rises. The heel should invert during liftoff.

30.1.5 Palpation

30.1.5.1 Lateral Ankle

The fibula is readily palpable and is a reference point for the lateral structures. Just posterior to the fibula are the peroneal tendons, peroneus longus, and brevis. The peroneus brevis is deep to the longus (remember the mnemonic "*brevis to bone*"). Their course is palpable down the lateral calcaneal wall. Peroneus brevis runs dorsal to peroneus longus, which remains plantar as the tendons course distal to the lateral malleolus. Peroneus brevis inserts at the base of the 5th metatarsal and is primarily responsible for foot eversion, which is counteracted by the inversion of the PT. Peroneus longus inserts at the base of the 1st metatarsal and is primarily responsible for 1st metatarsal plantar flexion and is counteracted by the dorsiflexion of the tibialis anterior.

The intermediate branch of the superficial peroneal nerve, in patients without significant swelling, is visible anterolaterally at the ankle and on the dorsal midfoot when the ankle is plantar flexed and inverted. It is the only peripheral nerve in the human body that is visible on normal surface anatomy [3].

30.1.5.2 Medial Ankle

The medial malleolus is the reference for all medial structures. As the medial malleolus is traced laterally and superiorly, the medial soft spot is felt, representing the medial gutter and Notch of Henry. By dorsiflexing the great toe and foot, respectively, the extensor hallucis longus and tibialis anterior tendons can be felt which is useful when performing a medial-sided ankle injection in this soft spot. The saphenous nerve courses just medial to the ankle joint at this level, and care should be taken to avoid the nerve with procedures such as injections.

Posterior to the tip of the medial malleolus is the PT. It can be felt along its entire course from proximally adjacent to the tibia to distally along its insertion on the navicular. Approximately one fingerbreadth posterior and superior to the medial malleolus, one can palpate the posterior tibial artery as it courses through the tarsal tunnel.

Deep and less palpable are the flexor digitorum longus (FDL) and the flexor hallucis longus (FHL). "*T*om, *D*ick, *a*nd *v*ery *n*ervous *H*arry" is a common mnemonic denoting the order from anterior to posterior of the P*T*, F*D*L, *a*rtery, *v*ein, *n*erve, and F*H*L.

30.1.5.3 Posterior Ankle

The major structure is the Achilles tendon which inserts broadly upon the calcaneus. The tendon receives contributions from the medial and lateral gastrocnemius and soleus. Plantaris, which does not contribute significantly to function, inserts on the medial calcaneus on its long course from its origin on the posterolateral proximal tibia.

30.1.5.4 Anterior Ankle

The reference point for the anterior ankle is the tibialis anterior (TA). It can be felt with passive foot dorsiflexion. From medial to lateral, the tendons of the extensor hallucis longus (EHL), extensor digitorum longus (EDL), and occasionally the peroneus tertius may be felt by isolating their actions. The dorsalis pedis artery and deep peroneal nerve course between the EHL and EDL tendons.

30.1.6 Seated Examination

The examiner should take special note of the hair (especially loss, indicating decreased microvascular blood flow), temperature, and any scarring or calluses. The capillary refill of the toes should be tested (normal <2 seconds) and pulses of the dorsalis pedis and posterior tibial arteries felt.

Individual peripheral nerves may be evaluated for proper function. The tibial nerve may be assessed as it passes behind the medial malleolus with gentle percussion, with distal paresthesias indicating a Tinel sign (a common term for such an exam in other areas of the body).

Range of motion and stability should be noted in all joints of the foot and ankle. The ankle normally medially deviates during plantar flexion (PF) and laterally deviates during dorsiflexion (DF). Normal DF is 10–15° and normal PF is 45–50°. Isolation of tibiotalar motion is accomplished by inverting the heel to lock the transverse tarsal joints. The anterior talofibular ligament (ATFL) may be assessed via the anterior drawer test in plantar flexion and the calcaneofibular ligament (CFL) via the anterior drawer test in dorsiflexion inversion stress test. Subtalar motion is measured by inversion and eversion of the heel and denoted either in degrees or a percentage of normal. The ankle and subtalar joints have linked motion, as the subtalar joint has one degree of eversion for each degree of ankle dorsiflexion and one degree of inversion for each degree of ankle plantar flexion. When assessing the transverse tarsal joints (talonavicular and calcaneocuboid), the adduction-abduction ratio should be 2:1. Midfoot range of motion is more limited on examination, with the medial tarsometatarsal (TMT) joints having less range of motion than the 4th and 5th TMT joints.

30.2 Appropriate Radiographic Evaluation of Foot and Ankle Problems

Advanced imaging options offer detailed anatomic and biologic views. Cost-effective use of imaging must either confirm a clinical suspicion or change clinical management.

30.2.1 Radiographs

Most imaging workup will begin with plain radiographs. Whenever possible, these radiographs should be weight bearing. They include an AP, lateral, and mortise (Figs. 30.2, 30.3, and 30.4). For the foot, an AP, oblique, and lateral view are standard.

Several other views exist and may be useful in the diagnosis of different pathologies. These include the ankle impingement views in the extremes of plantar and dorsiflexion and stress views of the syndesmosis. Many common foot and ankle pathologies, such as strains or sprains, may resolve without incident. Thus, the Ottawa Ankle rules serve as useful guidelines for obtaining advanced imaging. Essentially, if the patient

Fig. 30.2 Anteroposterior (AP) view of the right ankle

Fig. 30.3 Internal rotation (mortise) radiograph of the right ankle. Note that this radiograph more clearly demonstrates the joint space

has bony tenderness or inability to bear weight for at least four steps, an X-ray series should be obtained [4].

30.2.2 Ultrasound

Ultrasound can be a useful adjunct in diagnosis of foot and ankle pathologies. Advantages include its ability to provide dynamic imaging in a low-cost, radiation-free manner. It is, however, limited by the ability to penetrate materials such as bone, hardware, and gas. Clinically, ultrasound is used to assess ganglion cysts and superficial structures. When the probe is passed over a painful structure, sonopalpation provides visual confirmation to diagnosis.

Fig. 30.4 Lateral radiograph of the ankle

30.2.3 Computed Tomography

Computed tomography (CT) is useful in delineating bony anatomy in the three anatomic planes: coronal, sagittal, and axial. This is of particular value in surgical planning for complex fractures of the foot and ankle, especially midfoot fractures and dislocations, Tillaux fractures, and pilon fractures. It is also a useful imaging modality to assess for bony union in fusion procedures.

30.2.4 Magnetic Resonance Imaging

Commonly used sequences are T1, T2, and fat-suppressed images. Briefly, T1 images delineate anatomy in high resolution, T2-weighted are fluid bright and detect inflammation and edema, and fat-suppressed images are a useful adjunct for further characterizing lesions.

Ligaments appear dark and often lie oblique to the axis of imaging. Strains appear as signal hyperintensity within the ligament with thickening or possibly edema versus a discontinuity in

fibers with tears (Figs. 30.5 and 30.6). MRI is not routinely used for sprains except in determining extent of midfoot ligamentous injury (as found in Lisfranc injuries) and helping the clinician determine whether to proceed with exam under anesthesia. It should be noted that CT is also a very sensitive and less costly modality for imaging the midfoot for these injuries [5].

Fig. 30.5 A T1-weighted sagittal MRI image of the ankle in a patient with an Achilles tendon rupture

Fig. 30.6 A T2-weighted MRI image in the same patient. Note that this fluid-sensitive sequence visualizes the significant amount of edema surrounding the injured tendon

MRI is also commonly used to characterize articular cartilage topography and assess for bone marrow edema found in osteochondral defects. Some special sequences such as T1rho and DGEMRIC sequences exist to quantify cartilage health, but their discussion is beyond the scope of this text.

Finally, MRI may be used to assess tendinous structures. Tendinosis may be visualized as an increase in signal intensity on T1 GRE sequences or peritendon inflammation on T2-weighted sequences.

30.3 Orthotics: Principles of Nonoperative and Operative Management

30.3.1 Alignment

Lower extremity alignment is fundamentally important in pain-free, normal gait and stance mechanics. The mechanical axis is defined in the frontal plane by a line drawn from the center of the femoral head to the center of the talus. It should intersect approximately 1 cm medial to the tibial plateau. Deviations from this normative value predispose to osteoarthritis in various joints of the lower extremity.

Below the knee, the anatomic and mechanical axes are parallel. The anatomic axis of any bone is defined by the line subtending two midpoints of the bone diaphysis. When viewed from behind, the calcaneus lies in slight valgus relative to the tibia. Sagittally, the axis of the tibia should intersect the center of the talar dome. Generally speaking, it is important for the foot to be plantigrade (as discussed earlier with the tripod of the foot). As a result, most deformities about the foot and ankle develop a secondary deformity (e.g., in pes planovalgus, the forefoot may be in varus). Understanding this concept allows the clinician to make modifications to shoewear and via orthotics to improve alignment.

30.3.2 Shoewear

In the adult foot and ankle, most deformities are acquired and may be the result of ill-fitting shoes. As a result, patient education and prescription of

proper shoewear, devices, and orthoses may be a cost-effective means of treating various problems. These include hallux valgus (bunions), hammer toes, hard corns, interdigital neuromas, and plantar keratoses.

When buying footwear, patients are advised to consider the recommendations of a joint panel from the National Shoe Retailers Association, Pedorthic Footwear Association, and the American Orthopedic Foot and Ankle Society. Main points include trying shoes on at the end of the day, leaving one fingerbreadth of space between the end of the shoe and the longest toe, and measuring the shoe in a weight-bearing position.

30.3.3 Orthoses

Orthoses attempt to correct the position of the foot and ankle by applying a controlled force to various anatomic structures. These can range from simple shoe inserts to ankle-foot orthoses (AFOs). Ultimately, the goal of these devices is to cushion areas that experience too much pressure, controlling the shape of flexible deformities, and to accommodate fixed deformities to more evenly distribute body weight in a more anatomic way. While these devices may be useful in alleviating pain, there is no evidence that they can prevent structural deformities.

Custom orthoses may be made of soft, semirigid, or rigid materials and may require adjustment of the depth of footwear for the patient to accommodate the orthosis. Soft materials are used for cushioning which is of particular importance in people with diminished sensation, such as in diabetic feet or neuropathy from other causes. Semirigid inserts offer structural support and impact absorption. As such, they can be used for flexible deformities by offering structure and modifying weight transfer. Finally, rigid orthoses control motion in rigid deformities that may accompany arthritis of the midfoot and forefoot. These are most commonly used to control over-pronation of the foot but may be uncomfortable in patients with fat pad atrophy or bony plantar prominences and should not be used in insensate patients.

Ankle-foot orthoses (AFOs) span from the mid-tibia down to the foot and may be made from double upright bars or polypropylene molded to the shape of the patient. The ankle portion of the device may be either fixed or hinged. They may be modified through reliefs over bony prominences or to provide comfort. By modifying the position of the trim lines in molded models, the orthotist may control the various joints of the foot and ankle.

30.4 Common Degenerative Problems of the Foot and Ankle and Their Management

End-stage ankle arthritis has been shown to be as disabling as hip arthritis on patient-reported outcome measures [6]. Because it is most commonly posttraumatic in etiology, ankle arthritis often has onset at an earlier age than either hip or knee arthritis and therefore affects an individual for a longer period of their life. Management of ankle arthritis in early stages consists of symptomatic management, either with bracing with a gauntlet or solid ankle-foot orthosis, potentially with a rocker bottom shoe, or limited use of corticosteroid intraarticular injection for symptomatic relief. When nonsurgical options fail, patient-centered discussions should be centered on ankle fusion (picture) or total ankle replacement (picture). While both ankle replacement and ankle fusion offer similar pain relief, ankle replacement offers improved gait pattern, stride length, and cadence [7]. On the other hand, ankle fusion offers a durable option with less likelihood of revision due to implant loosening or failure. Conventional wisdom suggests that younger more active patients are indicated for ankle fusion, while older patients with fewer demands on the components are better candidates for total ankle replacement. Age is not an absolute contraindication to either procedure; therefore a discussion of both options is relevant in most situations.

30.4.1 Common Neuropathic Problems of the Foot and Ankle and Their Complications

Diabetes is a devastating and growing problem in the United States [8] causing a host of problems from peripheral neuropathy to retinopathy to end-stage renal failure. Unfortunately, up to 68% of diabetic patients present with some form of foot or ankle pathology [9]. Impaired glucose management is known to result in damage to the vasa nervorum and is thought to do so by both accumulation of sorbitol and intraneural accretion of glycosylated byproducts [10]. This is currently an irreversible process that results in neuropathy and loss of protective sensation. Ultimately, the loss of proprioception both from neuropathy and retinopathy leads to postural increases in pressure which the insensate patient cannot feel. When combined with the presence of dysautonomia which accompanies microvascular changes, this can result in cracked skin that progresses to an ulcer or other repetitive microtraumas that can result in Charcot arthropathy [11].

30.4.2 Total Contact Casting

Total contact casting (TCC) remains a clinically cost-effective treatment strategy for grade 1 ulcerations. TCC is presumed to work by reduction of forefoot pressures by transfer of weight-bearing load to the cast wall. Studies are equivocal about the utility for TCC in heel ulceration with some studies revealing decreased heel pressures and some showing increased heel pressures [12, 13].

A few important principles in casting are to (1) not over pad as this can lead to shifting in the cast, (2) limit toe motion to diminish metatarsal head pressure, (3) to pad bony prominences experiencing increased pressure, (4) position the foot in a plantigrade position in the cast, and (5) change the cast in 5–10 days.

30.4.3 Tarsal Tunnel Syndrome

Tarsal tunnel syndrome is a compressive neuropathy of the posterior tibial nerve or its terminal branches within or as they exit the tarsal canal. The tunnel itself is behind the medial malleolus and is bordered by the tibia anteriorly, the posterior process of the talus laterally, and the flexor retinaculum medially. The posterior tibial nerve gives off three branches (medial and lateral plantar nerves and the medial calcaneal nerve) as it courses through the tunnel.

Patients with tarsal tunnel syndrome typically complain of burning, shooting, or electric-type pain most prominent at the medial ankle and plantar foot. As with any compressive neuropathy, it can be caused by a space-occupying lesion or may result insidiously after a trauma or be idiopathic in nature.

The diagnosis may be suggested by exam findings of a positive Tinel's sign over the course of the posterior tibial nerve and confirmed with electrodiagnostic (EMG) studies. While some debate exists, the sensory nerve conduction velocity is thought to be about 90% sensitive for confirming the diagnosis when testing the abductor hallucis and abductor digiti quinti muscles [14].

Treatment consists of both nonsurgical and surgical options with the choice of treatment dictated by the cause of neural compression. Space-occupying lesions may simply be excised whereas tarsal tunnel syndrome of other causes may be adequately treated with NSAIDs, multimodal pain regimens, or steroid injections adjacent to the posterior tibial nerve. When all nonoperative modalities have failed or if a structural problem exists, surgery is warranted. Any space-occupying lesion should be removed with care to not damage the nerve. Correction of deformities may provide indirect compression without need for nerve release. Surgical release of the posterior tibial nerve involves release of the flexor retinaculum with care to identify the nerve throughout its course and protect it.

30.4.4 Neuroma

Interdigital neuromas are a common source of pain in the foot. They are not always associated with a mass or inflammation but rather compression of the interdigital nerves which branch from the medial plantar nerve (MPN). The exact etiology of interdigital neuromas is not clear but may be a combination of anatomic, traumatic, or other extrinsic factors. Anatomically, the third webspace experiences greater mobility due to the relatively fixed position of the medial three rays and the relatively mobile nature of the lateral two rays. This may predispose the nerve, which lies below the transverse metatarsal ligament, to greater daily microtraumas. Other trauma such as falls, crush injuries, or transection may cause interdigital neuroma. Finally, processes that cause pressure against the nerve may result in interdigital neuralgia. Thickening of the transverse metatarsal ligament can cause pressure on the nerve as can fracture of the metatarsal.

Regardless of the cause, patients commonly report pain in the plantar aspect of the foot with radiation to the toes in several patients. This is aggravated by tight-fitting shoes or by prolonged dorsiflexion of the toes as in walking.

MRI may not be a cost-effective diagnostic modality in diagnosing this condition with some studies demonstrating lack of correlation between MRI findings and symptoms in one-third of the patients and others demonstrating favorable surgical results with transverse measurement of nerve greater than 5 mm. MRI may be useful in providing anatomic detail to rule out other causes of pain in the area such as degenerative joint capsule [15, 16]. Local anesthetic injection may be useful in relieving pain although interpretation of this should be done with caution as it may relieve pain as a result of other anatomic structures in the area (fat pad, plantar plate) [17]. Additionally, the use of cortisone may cause atrophy of the collateral ligaments or other collagenous structures and the plantar fat pad [18].

Morton's neuromas, which affect the interdigital nerves, may be treated with a wider shoe and a metatarsal pad. If a patient has failed all nonoperative management options, a dorsal approach is typically selected to prevent painful scar on the weight-bearing surface of the foot. The transverse metatarsal ligament is transected, and the nerve is freed proximally to the metatarsal head and excised. Rungprai et al. reported good results from burial of the nerve intramuscularly.

30.5 Common Soft Tissue Injuries of the Foot and Ankle and Their Management

30.5.1 Lateral Ankle Instability

Lateral ankle instability is a very common condition, with ankle sprains occurring an estimated 23,000 times a day in the United States [19, 20]. Activity in sports, cavovarus alignment, and ligamentous laxity are all risk factors for sustaining recurrent ankle sprains and developing chronic lateral ankle instability.

Nonoperative treatment consists of physical therapy with proprioceptive training and peroneal strengthening. Any cavus alignment merits considering a lateral forefoot posted foot orthotic to realign the deformity. A lace-up ankle brace can also serve as an adjunct in the healing process. Functional, active rehabilitation is key for rapid and effective healing.

If nonoperative treatment fails, surgical options are considered. Lateral ankle ligament reconstruction, such as the modified Brostrom-Gould procedure where the inferior extensor retinaculum is imbricated over the repaired anterior talofibular and calcaneofibular ligaments, is a common option for primary surgical treatment. If severe cavovarus malalignment exists, surgical correction through realigning osteotomies is a consideration.

30.5.2 Achilles Tendon Injuries

The Achilles tendon sees the highest load of any tendon in the human body, up to ten times body weight [21]. As a result, the Achilles tendon is subject both to acute rupture and chronic degenerative conditions.

Achilles tendinopathy occurs either at the insertion of the Achilles tendon at the calcaneus or in the non-insertional region of the tendon between 2 and 5 centimeters proximal to the insertion, where the tendon both has a watershed area of decreased vascular supply [22] and a torsional twist that allows it to store energy [23]. With aging, Type I collagen in the tendon decreases, and tendon fibril diameter decreases, leading to decreased flexibility of the tendon [24]. The mainstay of Achilles tendinopathy is stretching exercise by the patient of the gastrocsoleus complex. A heel lift in the shoe decreases stress on the tendon during daily activity. Nitroglycerin patches, cut to the size of the symptomatic area and applied directly to the skin on a daily basis, also have been shown to increase blood flow to the tendon and promote long-term healing [25]. After failure of nonoperative options, often after at least 6 months' trial, surgical options include gastrocnemius recession and debridement of severely diseased tendon, either through open or endoscopic techniques.

Achilles rupture is most commonly an injury of the middle-aged athlete performing jumping or similar activity, although it can affect all ages, both athletes and nonathletes. Similar to the region of non-insertional tendinopathy, Achilles rupture most commonly occurs in the watershed area between 2 and 5 centimeters proximal to the insertion (Figs. 30.5 and 30.6). Nonoperative treatment is often successful in healing Achilles rupture for individuals of all functional levels, with randomized controlled trials supporting good outcomes compared to operative management [26]. Other studies have also shown benefits of operative treatment for long-term strength of plantar flexion by up to 18% [27]. Operative treatment can be performed with suture methods through open, mini-open, or percutaneous methods. The rehabilitation for operatively and nonoperatively treated Achilles tendon ruptures is typically the same, using a functional rehabilitation protocol, with early weight-bearing and range of motion, avoiding dorsiflexion past neutral ankle position for the first 6 weeks.

30.5.3 Plantar Fasciitis

Plantar fasciitis is a relatively common cause of medial heel pain and tenderness. Patients characteristically complain of pain with their first steps in the morning and lessening with activity. Patients typically localize the pain about the medial tubercle of the calcaneus. Through a mechanism known as the windlass mechanism, dorsiflexion of the toes will increase tensile forces on the calcaneal aspect of the plantar fascia and therefore pain. Treatment is almost always nonoperative with improvement or elimination in pain noted with maximizing length of the gastrocnemius/soleus complex [28, 29]. Corticosteroid injection may provide temporary relief of pain [30] but typically does not provide sustained relief and is also accompanied by complications such as plantar fascia rupture and fat pad atrophy [31]. The literature has not proven the effectiveness of extracorporeal shock wave therapy. Finally, gastrocnemius recession may be used after extensive nonoperative treatment has failed to provide adequate relief [32].

30.5.4 Posterior Tibial Tendinitis

Tendinitis of the PT can lead to adult flat foot deformity and is staged according to the severity of symptoms and deformity. It was first classically described by Johnson and Strom as having three stages [33]. It is ultimately a degenerative process that begins with tendinitis/tendinosis of the PT tendon and progresses to dysfunction of the tendon and inability to perform single heel rise, followed by eventual collapse of the spring ligament and resultant collapse of the arch and stiff flat foot. The stages and their respective treatments are cited in the table below as modified from the JAAOS article by Deland from 2008 [34] (Table 30.1).

Table 30.1 The stages and their respective treatments are cited in the table below as modified from the JAAOS article by Deland from 2008 [34]

Stage	Deformity	Physical exam findings	Radiographic findings	Treatment
I	Tenosynovitis, may have preexisting pes planus but without deformity	Able to perform single heel rise (SHR)	Essentially normal	Rest, NSAIDs, PT strengthening, CAM boot
IIA	Mild/moderate flexible deformity (can be passively corrected)	Inability to perform SHR	<30% talonavicular (TN) uncoverage, collapse of Meary's angle and longitudinal arch	Consider medial forefoot posted custom AFO, gastrocnemius stretching, PT strengthening
IIB	Severe flexible deformity	"Too many toes" sign (forefoot abduction) Inability to perform SHR Mild sinus tarsi pain	>30% TN uncoverage, arch collapse as in IIA	"All-American" procedure (calcaneal slide osteotomy to correct hindfoot valgus, lateral column lengthening to correct forefoot abduction, cotton osteotomy to correct forefoot varus)
III	Fixed deformity	Inability to perform SHR Severe sinus tarsi pain	Arch collapse with subtalar arthritis	Arizona bracing, double arthrodesis (subtalar/TN) vs triple osteotomy (subtalar, TN, calcaneocuboid) [35]

30.5.4.1 Fractures

Fractures of the foot and ankle are common and a potential source of significant morbidity. Given the wide array of possible osseous injuries in this anatomic location, detailed discussion of these conditions is outside the scope of this text. As a general principle, clinicians should consider obtaining plain radiographs of the foot and/or ankle in patient with significant bony tenderness (e.g., over the malleoli), ecchymosis, possible mechanism of injury, or inability to bear weight (Figs. 30.7 and 30.8).

30.5.4.2 Arthritis

As with fractures, the management of ankle arthritis is outside the scope of this text. Although less common than in other areas such as the hip and knee, degenerative changes at the ankle are a significant source of morbidity. Patients with ankle arthritis have activity-related pain, loss of motion, and functional deficits as seen in other anatomic locations. Radiographs demonstrate a loss of articular cartilage, associated subchondral sclerosis, and osteophyte (bone spur) formation (Fig. 30.9). Some patients' mild or moderate symptoms can be treated nonsurgically with injections, bracing, and footwear modifications. Patients who do not respond to less invasive modalities may benefit from ankle replacement (Fig. 30.10) or ankle fusion (Fig. 30.11). Ankle replacement (arthroplasty) is increasing in popularity but can be complicated by infection and loosening as in other joint replacement surgeries. Ankle fusion is a durable reconstruction that provides lasting pain relief for many patients. The loss of motion at the tibiotalar joint, though, can make patients more likely to develop degenerative changes elsewhere in the foot.

Figs. 30.7 and 30.8 AP and lateral radiographs of a fracture dislocation of the ankle. Note the significant disruption of the bony structures around the ankle as well as the significant lateral and posterior displacement of the talus

Fig. 30.9 AP radiograph of a patient with osteoarthritis of the ankle. Note the loss of joint articular cartilage (joint space) and bone spur formation

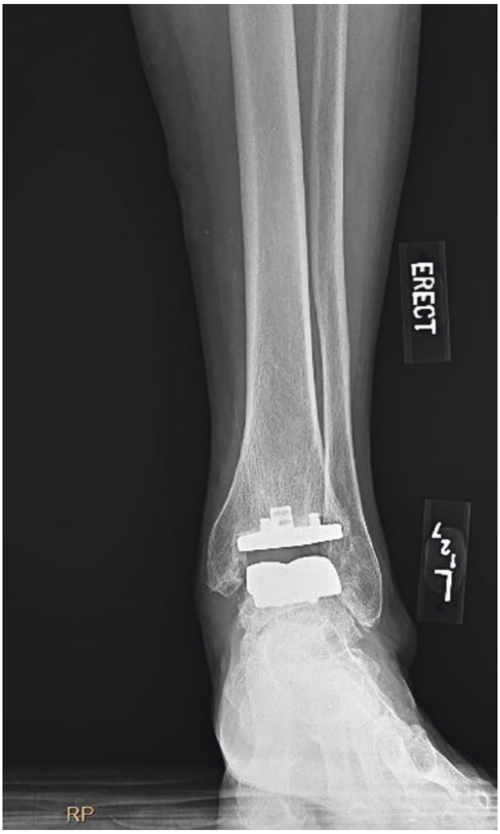

Fig. 30.10 AP radiograph of a patient after total ankle arthroplasty

Fig. 30.11 Lateral radiograph of a patient after tibiotalar (ankle) fusion

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